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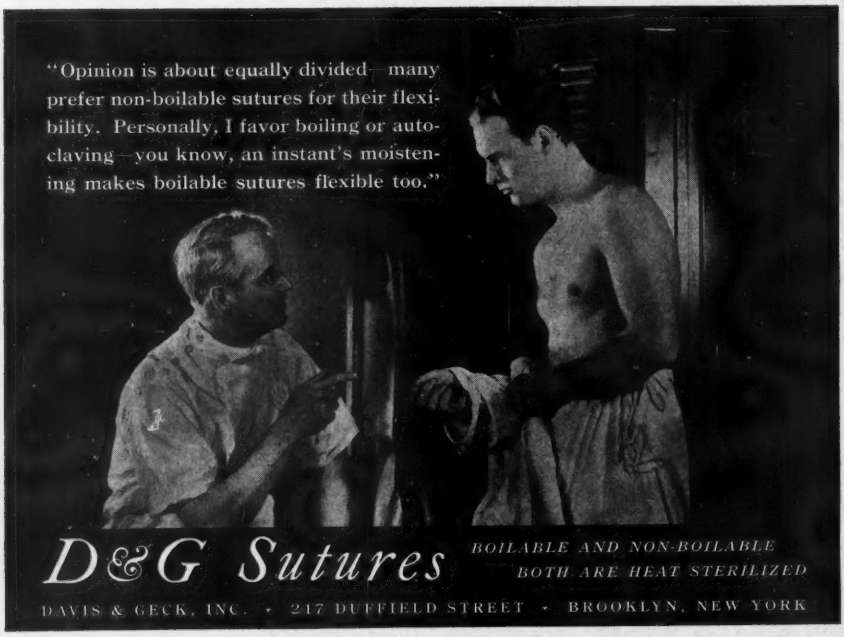
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Carl Arthur Hedblom

1879-1934

A former member of the Advisory Editorial Board of this Journal and a pioneer in the development of thoracic surgery.

UNIV. OF MICH.

The Journal of Thoracic Surgery

VOL. 3 AUGUST, 1934 NO. 6

Original Communications

IN MEMORIAM

Carl Arthur Hedblom

ON JUNE 6, 1934, Carl Hedblom, a member of the Advisory Editorial Board, died suddenly at Toronto while attending a meeting of the American Surgical Association. When the news reached me on the following day, it seemed hard to believe because those of us who had seen him at the meeting of the American Association for Thoracic Surgery in Boston just a few days before had observed no change in his customary physical and mental vigor. His death followed an illness of less than forty-eight hours and was due to coronary thrombosis. The news of his being suddenly struck down in the prime of life came as a blow to his many surgical colleagues and friends in this country and in Europe.

Dr. Hedblom was born in Dayton, Iowa, on March 5, 1879, the son of Swedish parents, Peter Hedblom and Maria Sophia Johnson Hedblom. He was one of eight children. After attending a country school and the Fremont Normal School, he attended Colorado College, from which he received the degree of A.B. in 1907. In the following year he was given the degree of Master of Arts from the same college. He was graduated from the Harvard Medical School in 1911 and served as interne and surgical resident immediately after that under Dr. Maurice Richardson at the Massachusetts General Hospital from 1911 to 1913. In 1920 he was given the degree of Ph.D. by the Mayo Foundation and in 1921 the degree of D.Sc. by Colorado College. Few surgeons have had the variety of experience which he has had. From 1913 to 1916 he was in China as Professor of Surgery at the Harvard Medical School at Shanghai. He returned to the United States in 1916 and became a Fellow at the Mayo Clinic, where he served in various capacities until 1924. During the last three years of his residence at Rochester, Minn., he was Associate Professor of Surgery of the Mayo

Foundation in charge of the division of thoracic surgery. He was then called to be Professor and Head of the Department of Surgery at the University of Wisconsin, where he stayed during 1925 and 1926. He left Madison to go to Chicago to become Professor and Head of the Department of Surgery of the College of Medicine of the University of Illinois, a position which he occupied at the time of his death.

He was commissioned in the army during the World War as Major with orders to sail for France at the time the Armistice was signed. These orders were canceled, and he therefore saw no active service in France.

Although Dr. Hedblom had extensive training and experience in general surgery, his interests became more and more confined to thoracic surgery, and in his later years all of his writings on surgical subjects pertained to that special field. Entering the field of thoracic surgery at an early stage of its development, he soon acquired an international reputation as one of the outstanding workers in surgery of the chest. His judgment was excellent and was tempered with the sound common sense upon which all good surgery is based. He was a careful operator without any particular flash of dexterity which so often deceives the onlookers into thinking that they are seeing superlative work. After seeing Hedblom operate one always felt that the work had been well done and that the patient's interests had been the object of chief consideration. There was nothing of the showman about him, and partly because of this fact he inspired the utmost confidence in his patients and colleagues from the standpoint of his thoroughgoing honesty and conscientiousness. He was dignified, modest, unassuming and had no trace of pretense or of those qualities which are often included in the expression "front." When he addressed medical meetings, his audience always very properly felt that he was speaking from an honest conviction based on an extensive study of his subject. His conclusions as well as his virile physique were based on solid ground.

His chief contributions to thoracic surgery were of a sort which are always badly needed during the early years of the development of a new field when false leaders and wild ideas are likely to steer the ship on a wrong course. They were largely statistical studies of his own and others' experiences from which he was able to draw conclusions which doubtless prevented many a younger surgeon from chasing a rainbow with certainly harmful results to the patients concerned. Probably his most important contribution to thoracic surgery was his pioneer work in the making of thoracoplasty a multiple stage operation. It is difficult now for those who did not realize the trend of thought a few years ago to realize fully the opposition to his sound dictum that a multiple stage operation meant a lower operative mortality and also widened the possibility of the application of thoracoplasty to patients who otherwise might not be suitable risks. Experi-

ence has shown that he was right. His contributions to the subject of chronic nontuberculous empyema are also deserving of high praise. Probably we owe to him more than to any one else the present realization of the fact that it is better to postpone radical operations for chronic empyema until after a period of really adequate drainage has been established for perhaps even two or three months. Others had recognized this fact, but Hedblom emphasized it in so forceful a manner that his paper published in the *Annals of Surgery* in 1920 must remain a classic on this subject.

From the early days of the formation of the American Association for Thoracic Surgery, Hedblom took an active part in the affairs of the organization. In 1924 he served as President of the Association. With the beginning of the JOURNAL OF THORACIC SURGERY in October, 1931, he became a member of the Advisory Editorial Board, and his counsel was much sought by the Editor on various questions. In 1923 the Association met in Chicago at his invitation and enjoyed one of its best meetings. Again at his invitation, it had been planned to hold the next meeting of the Association at Chicago, but as an indication of the affection which the members of the Association had for him it was decided that the proper atmosphere for a meeting there could not be developed so soon after his tragic death.

To Carl Hedblom's personality it is difficult for this one of his intimate friends to pay as adequate tribute as he would like to do if he were endowed with a better gift of expression. He had a charming smile and a hearty laugh which captivated every one because it radiated his innate kindliness and charity. Completely lacking in fraud himself, he could scarcely understand that any one else could be insincere. He was therefore never harsh or vitriolic in his criticisms or disagreements in discussion. When he had a disagreement with some one, he was inclined to think that the other view was sincerely mistaken, but he was willing to change his own ideas if sufficient evidence could be produced that he was wrong. His vigorous, massive physique, combined with his kindly smile, seemed to make him exude friendliness, and the large number of his admiring friends bears witness to that fact. He cared little for formal society, and he did not engage in athletics or competitive sport for recreation. He enjoyed travel and good literature, but nothing was allowed to interfere with his work, at which he seemed tireless. He was an inspiring leader to his subordinates because of both his ability and his character.

In 1930 he acquired a serious streptococcal infection of his right index finger while operating on a patient with empyema. This infection developed into a virulent septicemia and almost caused his death, but after an illness of several months he was able to return to his surgical work with apparently no loss of skill in spite of a serious crippling of that finger.

In 1911 shortly before completing his service at the Massachusetts General Hospital, he was married to Eleanor Pease, who with three sons and a daughter survive him. His aged mother in her ninety-second year is still living, as are also one brother and six sisters.

The bibliography of his contributions to thoracic surgery is appended.

Evarts A. Graham.

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Alexis Victor Moschocowitz*

1865-1933

OUR Association has lost one of its most valued and beloved members through the death of Alexis Victor Moschcowitz. While he was especially known in thoracic surgery for his work with the Empyema Commission during the World War, he has made two important and original contributions to the surgery of the chest wall.

His outstanding clinical discovery concerning infections of the costal cartilages is well known. It was published in the *Annals of Surgery,* vol. 68, page 168. He found that in order to eradicate this disease it is necessary to remove the entire affected cartilages, sometimes a truly radical and major procedure but one which surgeons have recognized more and more as the only certain method for dealing with this obstinate pathologic condition.

His latest contribution was the recognition and description of the hitherto unknown vestigial mastitis which had long been the subject of unsuccessful investigation by others, and which he presented before the American Surgical Association at its meeting in 1933.

His faithful adherence to the Carrel method of treating suppuration of the pleura by meticulously following the method of its originator resulted in a large proportion of cures with a minimal number of operations.

In general surgery Dr. Moschcowitz was a distinguished figure. His writings on the surgery of hernia and of prolapse of the rectum are known throughout the medical world, and it is gratifying to know that he had the good fortune to be recognized as a master during his lifetime.

*Read at the Seventeenth Annual Meeting of the American Association for Thoracic Surgery, Boston, Mass., May 31, June 1 and 2, 1934.

His scientific vocation began with his graduation in pharmacy in 1885. He received his medical degree in 1891 when he was awarded one of the Harsen prizes of the College of Physicians and Surgeons of Columbia University.

His hospital appointments were many, and wherever he worked his influence was for the better development of his profession. At the same time he made himself affectionately admired and respected by all with whom he came in contact.

In 1927, he became a Fellow of the Royal Academy of Physicians of Rome. He was an enthusiastic Fellow of the Société Internationale de Chirurgie, and none of its Congresses seemed complete without him.

At the time of his death in the zenith of his career he was Consulting Surgeon to Mount Sinai Hospital of New York and was connected with many other institutions in that city, in either an active or a consulting capacity. He held the rank of Professor of Clinical Surgery in the Medical Department of Columbia University.

The personality of Alexis Moschcowitz was truly a charming one, full of friendliness and humor. Whenever he spoke, his hearers were instructed by his message and entertained by its delightful presentation.

Howard Lilienthal.

THE DEVELOPMENT OF LOBECTOMY AND PNEUMECTOMY IN MAN*

GEORGE J. HEUER, M.D.
NEW YORK, N. Y.

I IMAGINE every man unexpectedly elevated to the presidency of an important association has a period of reflection. He begins by contemplating himself and wonders at his elevation to this high office. He passes on to consider his friends and associates who have so signally honored him and whose high achievements so dwarf his own. He meditates upon the history of the society he temporarily represents, its honored past, its vigorous present, and its promising future, and dedicates himself to its welfare. He writes what is dignified as an address which because of his previous reflections commonly considers some historical aspect of the association or of its work and problems. To this point I have arrived; and with your permission, I shall speak to you, largely from an historical viewpoint, of the development of lobectomy and pneumectomy in man. As a subject it is as alive, as eagerly pursued and its further development perhaps as hopeful as many others with which this association has to do.

When and by whom the first deliberate lobectomy in man was performed, I have not been able certainly to determine. Stephen Paget[1] in his *Surgery of the Chest* states that Rolandus[2] performed a lobectomy in 1499 and Tulpius[3] in 1624. They were cases of accident in which the lobe herniated through a wound in the thoracic wall, and in both of which the herniated lobe was amputated with success. In the years between 1836 and 1880 there are the records of Forde,[4] Hale,[5] Grinnell,[6] and Richards[7] who similarly and with success removed a lobe or part of a lobe which had herniated through an accidental thoracic wound. I have failed to find that a deliberate lobectomy for any disease of the lung was performed before 1880.†

I refer to this year because it marked the beginning of scientific experimental work on lobectomy and pneumectomy. In 1881, Gluck[8] reported his experiments on pneumectomy. In six dogs and fourteen rabbits he removed the lung after tying a mass ligature around the hilus. All the dogs died as did a number of the rabbits, but two rabbits lived for three months. Death was due to septic pleurisy, pericarditis,

*Presidential address before the Seventeenth Annual Meeting of the American Association for Thoracic Surgery, Boston, Mass., June 1, 1934.

†Péan in 1861 during the resection of a tumor of the third, fourth and fifth ribs removed a portion of the lung.

and pneumothorax. Remarkable dyspnea and cyanosis followed some of the operations. In animals which lived a sufficient time he found the bronchial stump well healed. He concludes that if the technic is perfect, recovery from pneumectomy is permanent. In this year and almost simultaneously appeared the work of Block[9] and Schmidt.[10] Block, first informing himself in the methods of Lister at the clinics of Kuester and Volkmann, extirpated the lung in five rabbits and four dogs after ligation of the hilus. The rabbits died for the most part immediately after operation, the dogs some days after operation. One dog lived fourteen days. Later he attempted some further experiments and under the most rigid antiseptic technic removed the lungs in four dogs. As in the previous experiments they all died of a hemorrhagic fibrinous pleuritis. In spite of his unfortunate experience he states that the possibility of total lobectomy or pneumectomy is established and that the operation is applicable to man. Hans Schmidt reported his experiments on resection of the apex of the lung in dogs. He resected the fourth and fifth ribs, drew the apex of the lung into the wound, controlled it with a constricting ligature, amputated it, tied off the cut surface, removed the constricting ligature, and closed the wound. In the absence of aseptic technic four of the eight animals so operated upon died of sepsis and one of acute carbolic acid poisoning. Biondi[11] in 1882 performed pneumectomy in fifty-seven animals with thirty recoveries; by far the best results which had been achieved. Two years later he reported the results of lobectomy or pneumectomy in ten rabbits, six cats and five dogs previously infected with pulmonary tuberculosis. His results were less successful. Excluding about half the animals which died after the tubercle bacilli were injected there was a higher incidence of postoperative infection in the remaining animals subjected to lobectomy. His thesis, that lobectomy might prevent the spread of tuberculosis from one lobe to the adjacent lobes, seemed indicated to him from his experiments.

I quote these early experiments to show how suddenly the experimental approach to the problem of lobectomy and pneumectomy came into being. To relate in detail the experimental work which followed would carry me far beyond my time, but I cannot permit myself not to mention the names with the references of those who prosecuted it. J. B. Murphy[12] (1898), Tiegel[13] (1907), Friedrich[14] (1907), Samuel Robinson[15] (1908), Halsted[16] (1909), Willy Meyer[17] (1909), Robinson and Sauerbruch[18] (1909), Mollgaard and Rovsing[19] (1910), Schlesinger[20] (1911), Garré[21] (1912), Lenhartz[22] (1898), Schepelmann[23] (1913), Henschen[24] (1914), Giertz[25] (1914), and Kawamura[26] (1914) all studied the subject by the experimental method and made contributions to it. In connection with this important work the question of anesthesia arose,

particularly with reference to the advisability of negative or positive anesthesia in intrathoracic operations. In this field the names of Sauerbruch,[27] Robinson,[28] Willy Meyer,[29] and Meltzer and Auer[30] hold a prominent place. From the survey of this work, I may say that the results were as follows: (1) Positive pressure anesthesia in intrathoracic operations was found to be satisfactory and supplanted negative pressure anesthesia. (2) A very high incidence of infection among workers even after the aseptic period seemed to indicate that the pleura was quite susceptible to infection. A comparatively few workers, notably Halsted, Willy Meyer, and Kawamura successfully overcame this complication. (3) A number of methods of treating the bronchial stump were found which in the dog and smaller experimental animals proved successful. (4) It was noted by many investigators that there was little alteration in the pulse and heart's action after pneumectomy, but no very accurate studies of pulse and blood pressure or of subsequent changes in the heart had been made. (5) The question of the pleural exudate which formed so commonly after operation was left in doubt. It was thought by some to be the result of positive pressure anesthesia. In the experiments of the minority of observers it failed to occur. (6) It was found by some that the obliteration of the pleural cavity left after pneumectomy occurred through the expansion of the remaining lung; by others that some procedure such as rib resection was necessary to achieve it. (7) One author studying the anatomic changes in the lung remaining after pneumectomy found what he considered a true compensatory hypertrophy of this lung. (8) The effect of pneumectomy on the probable duration of life, and the physiologic compensatory changes in the lung remaining after lobectomy had not been determined.

It was because of the lack of agreement among the workers upon certain questions above outlined and the lack of information upon others that a group of workers including Cave, Dunn,[31] Emile Holman, Reichert, Rienhoff, Andrus and I again attacked the problem. The work was begun before the publication of Kawamura's work in 1914, was interrupted by the war, and was not published until between the years 1920 and 1923. This work served to clarify certain aspects of the subject in doubt and added some new information. Its results may be stated as follows: (1) Methods of closing the bronchial stump advocated by previous workers were tested and some new methods tried. It was found that certain factors such as the presence or absence of infection within the bronchus to be divided, the size of the bronchus and the rigidity of its cartilages, and the length of the bronchus which could be secured for closure all were of importance in the secure closure of the bronchial stump. It was determined that in the dog the bronchial stump could practically invariably be securely closed; because of the absence of infection within the bronchus (cultures of the mucosa as high as the

bifurcation were sterile)* and because the size and the length of the bronchial stump permitted a secure closure. (2) It was found in a series of 23 pneumectomies that there was little if any alteration in the pulse and blood pressure following the ligation of the main pulmonary vessels of the lung; and aside from the mild temporary increase in the respiratory rate there were no noteworthy changes in the respiration. (3) It was observed that if the lungs were kept moderately inflated the operation of pneumectomy if performed within the thorax could be carried out without affecting the cardiac action; but that undue traction upon the lung or upon the main bronchus commonly upset the heart-beat and if persisted in, caused a marked irregularity in its action. Examination of the animals up to a year after operation failed to show any considerable hypertrophy of the heart as stated by one previous worker; although in several instances a hypertrophy of the right ventricle seemed definite. (4) It was found that in the absence of infection a pleural effusion did not occur in the dog either immediately after or subsequent to the pneumectomy. This was a finding at variance with that of the majority of previous workers who described the formation of a clear or slightly turbid serous or serosanguineous effusion into the pleural cavity quite independent of an infection. (5) It was observed in all animals that the large intrapleural cavity left after the total removal of one lung rapidly became obliterated. The obliteration of the cavity began at once and within two weeks after operation was practically completed, although in some animals a small space between the base of the heart and the apical region and another between the lower border of the heart and costophrenic angle persisted for a longer interval. In the obliteration of the cavity the expansion or enlargement of the remaining lung is by far the most important factor, the other two factors being the retraction of the thoracic wall and the elevation of the diaphragm. Indeed, in the dog the capacity of the lung to enlarge is such that if a pneumectomy on one side is followed by successive lobectomies on the other, a single lobe of the lung will eventually enlarge to fill the entire thorax. (Figs. 1 and 2.) (6) The nature of the compensatory enlargement of the lung, so important in the obliteration of the intrapleural cavity, was not determined at the time our work was published. But the material was assembled and preserved. In the study it was of primary importance that the enlarged lung and the control were fixed at exactly the same degree of distention, and this part of the problem was solved by Reichert. Working with corrosion preparations of the bronchial and vascular trees of the control and the enlarged lung (six months after pneumectomy) he determined that there was no increase in the number of bronchi of the various orders down to the

*A study of the mouth bacteriology of nine dogs shows the presence in cultures of staphylococci, enterococci, colon bacilli and *Bacillus Welchii*. Smears from the human mouth always showed spirochetes and fusiform bacilli; in none of the smears from the dog's mouth have these organisms appeared.

terminal air sacs in the enlarged lung, nor was there an increase in the number of divisions of the arteries and veins. Rienhoff working from another angle of the problem constructed from serial sections wax models of the control and enlarged lung and a comparison shows that the im-

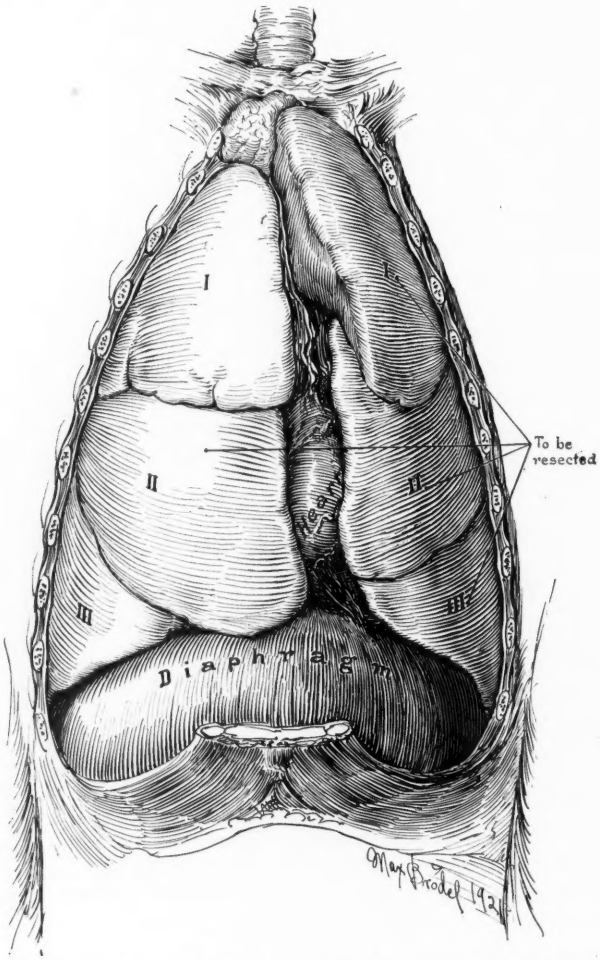

Fig. 1.—The thorax of a dog with its contents fixed in situ to indicate the position and size of the various lobes of the right and left lung. Personal observation 1919.

portant change giving rise in greatest measure to the compensatory enlargement is the dilatation of the atria, that part of the subdivision of the bronchial tree just proximal to the air sac (terminology of Miller). It would appear then without going further into detail (this work will

soon be published) that the enlargement of the lung is not of the nature of a hyperplasia or of any considerable hypertrophy but of a simple

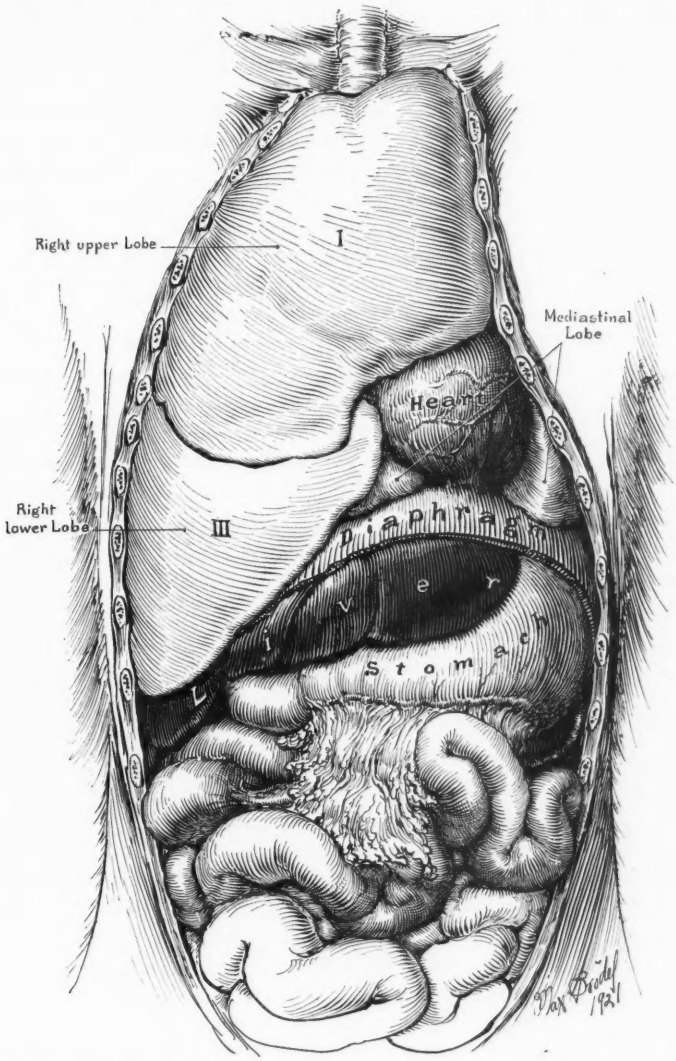

Fig. 2.—The thorax of a dog of the same size and weight with its contents fixed in situ six months after the removal of the lobes of the lung indicated in Fig. 1. It will be seen that the upper and lower lobes of one lung have expanded to fill the thorax. Personal observation 1919.

expansion largely the result of the dilatation of the atria and air sacs. (7) It was found that dogs kept a year or more after operation under

the same conditions as other animals suffered no ill effects from the removal of one lung. They were healthy, active, free from symptoms such as dyspnea, and in all respects seemed to hold their own with other animals. It appeared that pneumectomy would not seriously influence the probable duration of life. (8) It was found (Heuer and Andrus[36]) after pneumectomy that very definite changes occur in the alveolar air and blood gases consisting of a temporary increase in the alveolar CO_2, a fall in the alveolar oxygen, a slight increase in the CO_2 of the blood and a marked decrease in the blood oxygen; and by way of compensating for these changes until the enlargement of the remaining lung has taken place (thirty days) there is an increase in the number of red blood cells and hemoglobin and therefore an increase in the oxygen-carrying capacity of the blood. (9) It was found (Andrus[37]) that there were compensatory changes of a circulatory nature analogous to those just stated of a respiratory nature and consisted in an increase in blood flow and pulse volume to obviate the ill-effects of the temporary decrease in total lung volume.*

These findings seemed to establish without question the ideal pneumectomy. It consisted of a one-stage procedure under proper anesthesia in which a direct approach to the lung by a long intercostal incision, the isolation and division of the main vessels and bronchi and the secure closure of the bronchial stump was followed by the air-tight closure of the incision. Granting that the questions of infection and of the secure closure of the bronchial stump were eliminated by an adequate technic, the operation was without serious cardiac, circulatory or respiratory upsets and was followed by a rapid uncomplicated convalescence with the total obliteration of the intrapleural cavity by the enlargement of the remaining lung. Its advantages over multiple stage operations with all their trying details to surgeon and patient need not be pointed out to this assemblage. Its transfer to the human subject so far as its anatomic and physiologic effects are concerned seemed assured by accumulating experience.

Encouraged by the early experimental work on animals, surgeons began a deliberate attack upon the lung in man. Helferich[38] in 1898 removed two lobes of the lung for bronchiectasis with a fatal result; but Heidenhain[39] in 1901 performed a lobectomy in two stages for this disease with a successful outcome. Doyen[40] resected the apex of the lung for tuberculosis in 1886; and Kroenlein[41] removed a portion of a lobe for tumor in 1884. In the literature between 1880 and 1920, the period I have just covered for experimental work, I find records of 9 resections or lobectomies for tuberculosis, 14 for tumors of the lung or of the thoracic wall invading the lung, and 56 for bronchiectasis. I

*These findings have since been confirmed. Morrison,[32] Brit. J. Surg. 14: 94, 1926; Bettman et al.,[33] Surg. Gynec. & Obst. 46: 602, 1928; Adams and Livingstone,[34, 35] Arch. Surg. 25: 898, 1932.

shall not attempt to analyze these cases at this time. Brilliant as some of them undoubtedly were and showing the possibility of pulmonary surgery, the mortality in general was high, over 50 per cent, and the results in the patients who survived left much to be desired. These cases contributed largely to accumulating practical experience which was of predominant importance in determining the trend of the operative procedures in man. While the experimentalists were perfecting the ideal operation in the presence of normal conditions, surgeons were finding that the conditions created by disease were so far from the normal as to preclude the ideal operation. This was true to some extent of the tumors of the lung but was particularly so of bronchiectasis. Infections of the bronchial tree, adhesions of the lobe to the parietal pleura and diaphragm, a short, often indurated bronchial stump difficult of satisfactory treatment, debilitation and organ changes, the result of prolonged suppuration, all absent in the dog, were present in the human subject in this disease; and the attempt to perform the ideal lobectomy as is easily possible in the dog was followed by a high and indeed prohibitive mortality. The complications arising from the one-stage lobectomy were leakage of the bronchial stump, a particularly virulent type of suppurative pleuritis, mediastinitis, mediastinal emphysema, tension pneumothorax, postoperative shock, and so forth. The pioneers in lobectomy were led to the realization that due to the different conditions met with in man, surgical procedures other than the ideal lobectomy or pneumectomy had to be devised to meet these different conditions. From the early years of this century to the present time surgeons have exerted their ingenuity to devise surgical procedures to limit or to render less harmful the complications above enumerated. We have seen, therefore, the rise and development of the multiple stage operation. It would be interesting if there were time to describe in detail the various operations which have been developed, for they form a record not only of great ingenuity but of courage and untiring industry to relieve the sick of a terrible disease. The names of the men who contributed so largely to the development of lobectomy in bronchiectasis are listed in the table published by Ballon, Singer, and Graham[42*] in the JOURNAL OF THORACIC SURGERY. Their methods are also described, and in a later publication are again described by Alexander.[43] In various combinations of procedures and stages they attempt to isolate the part of the pleural cavity containing the lobe to be removed from the remainder of the pleural cavity so as to prevent the widespread pleural infection so fatal in earlier cases and to create conditions safe for drainage. This is done by provoking adhesions between the upper lobe of the lung and the parietal pleura by rubbing the pleura with gauze, by packing, by the cautery, and so forth. They attempt the removal of the lobe after this preliminary

*Graham's table has been corrected by me because the recent report of Jones does not correspond with Shenstone's figures.

stage in as rapid and simple a way as possible so as to avoid too prolonged manipulations within the thorax and to avoid opening up new pathways for infection in a cavity sealed off by the previous stage. The lobe is therefore removed immediately after the ligation of its pedicle without other attention to the treatment of the bronchial stump, or is allowed to slough away after the ligation of the pedicle. Its isolation—no simple part of the operation if there are dense adhesions between it and the surrounding structures—forms a part of the first or second stage according to the preference of the surgeon. Finally they attempt to obliterate an infected cavity by the resection of the necessary number of ribs as part either of the primary or of a later stage. In its simplest form this operation requires two stages, but it has required as many as five. It is a tremendous effort for the surgeon, a prolonged and harrowing experience for the patient.

We arrive then at the present, having seen in recent years an extraordinary interest and activity in lobectomy and pneumectomy for bronchiectasis and for tumors of the bronchi and lungs. In both groups of conditions we have as methods of procedure the one-stage and the multiple stage operation. In bronchiectasis in its very late stages we have the additional procedure of cautery pneumectomy. In the development of these procedures there has been the natural tendency to align ourselves on the side of the one-stage or multiple stage operation, to advocate the method we have devised or that which has given us the best results. The sum total of surgical achievements in bronchiectasis, confining our studies to the 16 cases collected by Willy Meyer[20] prior to 1914, 196 cases collected by Graham[42] between 1914 and 1931, and 13 cases collected recently, a total of 225 cases, show that 78 are cured and 31 probably cured, 24 are definitely improved, 9 are improved, 6 or more are unimproved, and 77 died from operation, a mortality of 34.2 per cent. The surgical results in the treatment of tumors of the bronchi and lungs which I have collected show that of 33 cases in which a lobectomy or pneumectomy was performed 20 recovered and 13 died, a mortality of 39 per cent; of 18 cases of pulmonary resection 5 died, a mortality of 28 per cent; and of 7 cautery lobectomies all died in from one to ninety days. The late results show that of the 20 cases recovering from lobectomy or pneumectomy, 14 died or were living less than one year, 1 had lived two years, and 1 five years. Two others are said to be cured. Of the 13 cases recovering from pulmonary resection, 11 lived less than one year, 1 lived more than one year, and 1 lived two years. The achievements of lobectomy and pneumectomy in bronchiectasis are considerable; those in tumors of the bronchi and lungs still leave much to be desired.

In a closer analysis of these results I shall exclude from the group of tumors just noted the cases of resection or fragmentary removal and

confine myself only to those in which a clear-cut lobectomy or pneumectomy was performed. Of the 33 cases so treated, 23 were subjected to a one-stage lobectomy, and 5 to a one-stage total pneumectomy. Of the total of 28 cases, 11 died within two months after operation, a mortality of 39 per cent. In 2 cases the wound was left open and was packed with gauze with a mortality of 50 per cent, in 3 cases the wound was closed about a gauze drain with a mortality of 66.6 per cent, in 11 cases the wound was closed with air-tight drainage with a mortality of 36.3 per cent, and in 4 cases the wound was closed completely without drainage with a mortality of 25 per cent. In 8 cases the method of closure was not given and the mortality was 50 per cent. In 16 cases from 3 to 7 ribs were resected before or after the lobectomy or pneumectomy to facilitate the approach or to obliterate the intrathoracic cavity. In 5 cases ribs were not resected, and in 7 the information is not given. It is interesting to note the fate of the intrapleural cavities in 4 of the 5 patients who recovered. In one case of lobectomy drained through a stab wound, the examination nine months after operation showed the lung filling the cavity, the diaphragm elevated and the heart dislocated toward the operated side. In 2 cases of complete pneumectomy closed without drainage (Rienhoff[44]) a small amount of serosanguineous fluid collected in the costophrenic sulcus which was aspirated; but since operation the remaining lung has enlarged to fill the entire thoracic cavity. This was to be expected from animal experiments.

An examination of the 5 cases classified as multiple stage lobectomies shows that in only 2 were multiple operations performed for the removal of the lobe itself. In these as in the multiple operations for bronchiectasis the first stage had for its purpose the production of adhesions between the other lobes and the parietal pleura. Of these 2 cases one patient recovered and one died. In the other 3 cases the preliminary operation consisted of a phrenicectomy or artificial pneumothorax, the lobectomy being done in one stage. There were two recoveries and one death.

It will be seen from this analysis that in the treatment of tumors of the bronchi and lungs by lobectomy and pneumectomy the one-stage operation overwhelmingly has been the operation of choice, having been used in 31 out of 33 cases. The mortality of the operation has been 38.7 per cent. The data are too few from which to draw conclusions, but from the evidence at hand the one-stage operation with closure of the thoracic wound without the resection of ribs has yielded the best results. It is the ideal operation as developed in experimental animals.

An analysis of the experience in bronchiectasis shows, contrary to that in tumors of the bronchi and lungs, how overwhelmingly the multiple stage lobectomy has been the operation of choice over the one-stage operation. The tabulation of Ballon, Singer and Graham[42] to which I

add the cases of Roberts and Nelson[45] recently reported shows that of 201 cases in which the information is available 146 were operated upon by the multiple stage operation, 55 by the one-stage operation. For long the multiple stage operation has been considered the safer operation and probably has been so in the past; but that it really is under the present changing conditions and that it will continue to be is open to question. If simply from a statistical viewpoint I assemble the cases of Graham's table into two groups, making the proper correction for more recent statistics and adding Roberts' and Nelson's cases, I find that in 55 one-stage lobectomies there was a mortality of 27 per cent; that in 146 multiple stage lobectomies there was a mortality of 37 per cent. I realize that this is an unfair comparison in favor of the one-stage operation, for it does not take into consideration the condition of the patient, the stage of the disease, and the conditions within the thorax. It is certain that among the cases operated upon in multiple stages are some which could not have been done in a single stage. I realize also that, according to the latest available figures, no individual surgeon's mortality with the one-stage lobectomy is yet so low as the lowest mortality achieved by an individual surgeon with the multiple stage lobectomy.*

What I wish to point out in all this is that in tumors of the bronchi and lungs we have approached the problem of lobectomy and pneumectomy in the direct and obvious way because conditions permitted it; while in bronchiectasis we have approached the problem in a circuitous way because conditions for the time being have made it necessary. It has been the history of the surgical treatment of many diseases that the conditions of the disease at the time it was first surgically attacked have made necessary operations which are but substitutes for the ideal; but with the acceptance of surgery by the profession and with earlier and earlier diagnosis and treatment, the conditions of the disease eventually permit the ideal. It is evident, I think, when one reads the protocols of recent lobectomies that the disease is being attacked in an earlier stage; that the conditions within the thorax are less difficult to manage and that therefore the one-stage lobectomy is becoming more possible. The trend away from the multiple stage operation and toward the one-stage operation has begun; for in no other way can one interpret the recent increasing number of cases treated by this method. There may be danger that we shall go too far in this direction and subject to operation in an early stage cases which are not of the true progressive type of bronchiectasis. As we study the disease by the newer methods we are coming to believe that the anatomic changes in the bronchial tree which we associate with bronchiectasis are often congenital and that these may exist for many years without the disease; and it is certain that a

*This statement is no longer true. I have information through correspondence that one surgeon has done 7 lobectomies for bronchiectasis by the one-stage method without a fatality.

respiratory infection with a purulent bronchitis superimposed upon dilated bronchi does not necessarily constitute the disease, for these attacks merely may be episodes in the life of an individual from which he recovers. We are in need at the present time of more information regarding the disease. Specifically we need more information than we now have in adults and particularly in children as to what cases may reasonably be expected to develop into the progressive disease we know as bronchiectasis. This information will probably eventually be forthcoming, for we may trust the conservatives among us to supply it.

Having brought ourselves to the present and having analyzed the status of lobectomy and pneumectomy in bronchiectasis and tumors of the bronchi and lungs it is but natural although hazardous to try to visualize future progress. It would seem to me that the trend inevitably will be toward the one-stage operation in bronchiectasis as well as in tumors of the bronchi and lungs. I foresee as a result, that many surgeons, lured by the simplicity of the one-stage operation, will be tempted to perform it without perhaps an adequate training in thoracic surgery, and with at least a temporary increase in the mortality rate. I imagine that many presumed cases of bronchiectasis will be subjected to operation which would not be according to our older conception of operative indications. I visualize the necessity, as I previously stated, of a further study and reconsideration of the disease, bronchiectasis, with the viewpoint of establishing new indications for operative therapy. I anticipate that new problems will become evident as each of us studies the results of his one-stage lobectomies or pneumectomies; or that a better solution of old problems will become necessary. One of the most important problems in lobectomy and pneumectomy—the aseptic division and secure closure of the bronchial stump—has been neglected during the period of the development of the multiple stage operation and in my opinion still is not satisfactorily solved. It again comes clearly into the foreground and to its solution we should continue to apply ourselves.

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THE EFFECT OF SUDDEN OCCLUSION OF EITHER PRIMARY BRANCH OF THE PULMONARY ARTERY ON CARDIAC OUTPUT AND PULMONARY EXPANSION*

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INTRODUCTION

THE circulatory disturbances which accompany changes in the mechanics of respiration are not completely understood. The belief that their importance has not been sufficiently emphasized in thoracic surgery stimulated us to begin a series of experiments of which those included in this report constitute the third part.

Our interest in this problem developed from a feeling of doubt as to the real cause of death in certain chest cases during or very soon after extensive thoracoplasty or some major intrathoracic operative procedure. It was our feeling that not infrequently respiratory symptoms receive an undue amount of attention because they are so obvious and so easy to interpret, whereas the true significance of circulatory changes, which are more obscure and harder to explain, is sometimes unappreciated or completely overlooked.

The predominant respiratory symptoms which are presented by such cases are dyspnea and anoxemia, the former being initiated by the mechanical impairment of ventilation (decrease in vital capacity) incident to the operative procedure, and the latter resulting from insufficient oxygenation of the blood as it passes through the lungs.†

The circulatory symptoms are a falling blood pressure, a rapid and thready pulse, generalized pallor and excessive diaphoresis—all of which are manifestations of a decrease in the circulatory blood volume and are generally accepted as signs of circulatory failure. The thought that

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†The more important causes of the decrease in vital capacity are resection of too much rib length at one time (with the resulting mobilization of a large area of chest wall which is pulled in during inspiration), pneumothorax, and plugging of bronchi by retained exudate and mucus. As a result the patient finds it necessary to expend more effort in order to maintain adequate expansion of the lungs. When because of weakness and exhaustion he is no longer able to do this and expansion becomes inadequate, the blood passing through the lungs is not sufficiently oxygenated and anoxemia results. The presence of anoxemia (oxygen deficiency of the tissues) is usually (but not always) indicated by cyanosis, the blue color being caused by the increased amount of reduced hemoglobin in the blood. The oxygen saturation of the arterial blood is the most accurate available measurement of the severity of this condition and the term anoxemia indicates a decrease in the percentage saturation of the arterial blood with oxygen.

circulatory insufficiency under the conditions described might be secondary to the very same mechanical causes which reduce vital capacity suggested to us that it would be interesting to alter the mechanics of respiration experimentally in different ways and observe the effects on the circulation.

Our researches began with a study of the circulatory effects of obstructive atelectasis of one entire lung in the anesthetized dog,[1] and later included a similar study of the effects of closed pneumothorax, partial occlusion of one primary bronchus, phrenicectomy and the respiration of nitrogen by one lung.[2] The results of these experiments have been published and will not be reviewed completely in this paper. However, we wish to call attention again to one of the most striking observations which was made, namely, the pronounced decrease in cardiac output which followed complete occlusion of a primary bronchus and total collapse of the corresponding lung. Decreases varying from 24 to 61 per cent were observed in eleven out of twelve experiments. This was accompanied by a partial shunting of blood out of the collapsed (blocked) lung into the opposite side, but the amount of blood shunted into the breathing lung was not sufficient to cause an increase in the amount of blood flowing through it. The circulation through the functioning lung was also reduced in eleven of the twelve experiments.

No explanation was offered by us for the decrease in cardiac output which was observed in these experiments, but coincident with the shrinking of the blocked lung one would expect the development of some degree of mechanical obstruction in the capillary bed, and the partial shunting of blood to the opposite lung, which was observed, indicated that this occurred. *Was the decrease in cardiac output caused by resistance to the flow of blood through the atelectatic lung?* If so, then ligation of one of the primary branches of the pulmonary artery and shunting of the total circulation through the opposite lung should be followed by a similar change. The experiments which are presented in this paper were undertaken to test this probability.

Incidentally it was observed in these experiments that occlusion of either branch of the pulmonary artery is usually associated with a change in the relative percentages of air respired by the lungs, and the significance of this change in relation to observations which have been made by others is discussed.

LITERATURE

Ligation of secondary branches of the pulmonary artery has been practiced clinically for the treatment of bronchiectasis (Sauerbruch[3] and Meyer[4]) and hemorrhage (Beye[5]); and ligation of the hilus of the left lung in a man with carcinoma of the bronchus, from whom the entire left lung was successfully removed, was recently reported by Graham and Singer.[39] Ligation of primary branches of the pulmonary artery has been the basis of many experimental studies. These studies,

which imitate in animals the condition of embolism of one branch of the pulmonary artery which sometimes occurs in man[6] include *measurements of systemic and pulmonary blood pressures,* Lichtheim,[7] Landgraf,[6] Gerhardt,[8] Plumier,[9] Tigerstedt,[10, 11] Kuno,[12*] Underhill,[13] Haggart and Walker,[14] and Scarff[15]; *measurements of pulmonary ventilation,* Churchill and Agassiz,[16] and Churchill[17, 18]; *the physical characteristics of the ligated lung,* Küttner,[19] Lichtheim,[20] Litten,[21] Landgraf,[6] Halsted,[22] Bruns and Sauerbruch[23] and Schlaepfer[24, 25]; and in some instances *measurements of the volume output of the heart,* Tigerstedt,[10, 11] Underhill,[13] Haggart and Walker,[14] and Drinker, Churchill and Ferry.[26]

The changes which follow occlusion of secondary branches of the pulmonary artery have also been studied experimentally, Bruns and Sauerbruch,[23] Kawamura,[27] Krampf,[28] Smirnoff,[29] and Mathes, Holman and Reichert.[30]

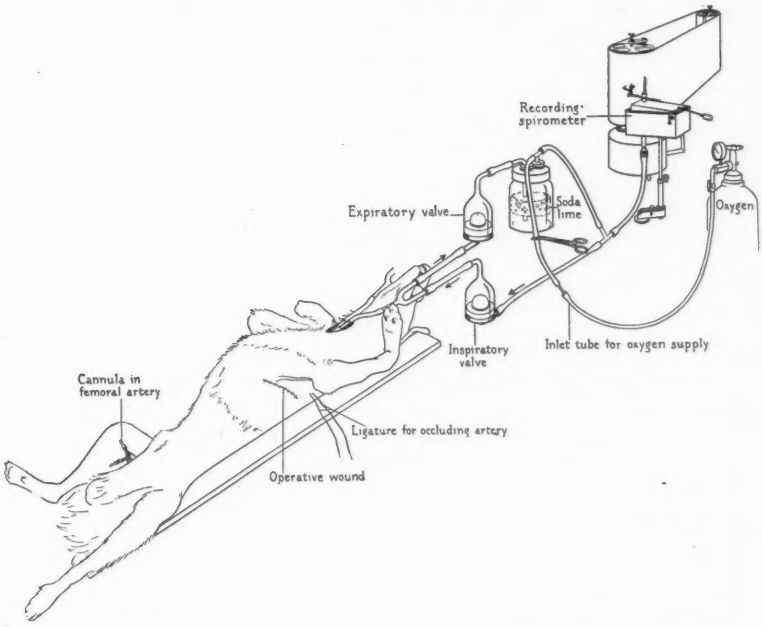

Fig. 1.—Showing the recording device and a complete drawing of the respiratory unit which was connected with the left lung. The recording spirometer in the right circuit was slightly larger than that in the left; otherwise the two systems were exactly the same.

METHOD

All the experiments were made on dogs which were anesthetized by the intravenous injection of barbital sodium and which breathed oxygen throughout the period of experimentation. The use of a specially constructed double barreled cannula, one arm of which was ligated in the left primary bronchus according to the technic originally described by Churchill and Agassiz,[16] permitted each lung to respire into a separate respiratory system. The details of the preparation have been described in previous publications,[1, 2] and are shown in the accompanying sketch of the new

*Kuno's observations were made after ligation of the entire hilus of the lung; whereas in the other experiments quoted in this series the artery alone was ligated.

apparatus (Fig. 1). Mercury seal valves similar to those described by Dr. C. V. Bailey[31] were recently substituted for the ordinary flutter valves because of their lower resistance.

The cannula now used (Fig. 2) consists of a small tube running through a large one rather than two tubes of equal size placed side by side. The new cannula provides a larger airway for the right lung; and since the tracheal wall can be more evenly apposed to a single cylindrical shaft than it can to a double one, the procedure for obtaining an air-tight seal in the neck has been simplified. It was also found that in using the old cannula in small dogs the right airway was sometimes obstructed by retraction of the stretched tracheal wall over the end of the tube. This effect is minimized by the new cannula.

When anesthesia was complete, the trachea was opened, cannula inserted, and artificial respiration begun. Then, after placing the animal on the right side, the thorax was opened through the fourth left intercostal space, and the end of the tube supplying the left lung was ligated in the bronchus well above the upper and middle lobe branches. After this a waxed ligature of braided silk was placed behind the artery to be occluded, and the ends were brought through the chest wall separately in the third intercostal space, anteriorly for occlusion of the left branch and posteriorly for occlusion of the right branch. When the bronchus had been

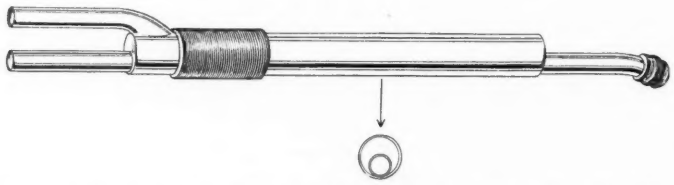

Fig. 2.—A drawing of the cannula which was used to separate the breathing. The smaller tube was ligated in the left primary bronchus, is 22.5 cm. long, and has an internal diameter of 7 mm. The larger tube, which served as an airway for the right lung, is 14 cm. long with an internal diameter of 13 mm.

cannulated and the arterial ligature was in place, the lungs were inflated and the chest was closed. Artificial respiration was discontinued immediately after this and the animal again breathed naturally. Separation of the breathing was made complete by compressing the tracheal wall against a rubber collar on the shaft of the cannula just below the tracheotomy opening. The artery could be occluded at any time simply by tightening the two ligature ends and tying them to each other on the surface of the chest wall.

When a dog lies on the right side, the left branch of the pulmonary artery is anterior to the veins and bronchus and can very easily be isolated just beyond the point where it emerges from the pericardium to enter the hilus of the lung. Isolation of the right branch is a difficult procedure and requires painstaking, sharp dissection. We have been most successful in isolating it by incising the pericardium at the base of the heart over the main stem of the pulmonary artery and then dissecting the cleavage plane between the artery and ascending limb of the aorta. The bifurcation soon comes into view and eventually, after cutting through the lateral pericardial reflection, the right branch of the artery is exposed extrapericardially just before it goes posterior to the ascending aorta to enter the right lung behind the vena azygos and pulmonary veins. Here the ligature can be placed behind it. Exposure of the right branch of the artery is helped by gentle traction on the main trunk. This can be conveniently applied by means of a clamp which grasps the fatty and connective tissue covering the artery.

When the preparation was complete, each lung was connected with a separate closed respiratory system, and the oxygen absorption and tidal air of each lung were measured separately from kymographic tracings. While these tracings were being obtained samples of arterial and mixed venous bloods were taken, the former through a cannula in the femoral artery and the latter by means of a special cannula[32] introduced into the right heart through a slit in the external jugular vein. The oxygen contents of the blood samples were estimated at once according to the manometric method of Van Slyke and Neill,[33] and the cardiac output was calculated according to the Fick formula,[34] namely:

$$\frac{\text{c.c. of oxygen absorbed per minute}}{\text{amount of oxygen absorbed by 1 c.c. of blood in passing through the lungs}} = \text{c.c. of blood passing through the lungs per minute}$$

The oxygen capacity (oxygen content of the aerated blood) was estimated also (venous blood samples being rotated for five minutes in a closed flask containing air at room temperature), and the percentage saturation of both the arterial and venous bloods was calculated by dividing oxygen content by oxygen capacity. When the arterial blood is 100 per cent saturated with oxygen, it necessarily follows that the same amount of oxygen is absorbed by 1 c.c. of blood passing through either lung. Under these conditions the volume of blood passing through each lung can also be calculated from the Fick formula and will be in the same ratio as the values representing oxygen absorption.

Observations made soon after the preparation was completed constituted the control studies. A few minutes later the pulmonary circulation to one lung was suddenly interrupted by pulling on the two ends of the ligature which had been previously placed behind the artery. The respiratory tracings made at this time constituted graphic evidence of whether or not the artery had been completely occluded because a lung without a pulmonary blood supply cannot absorb oxygen. Whereas previously the respiratory curve of this lung gradually dropped as oxygen was taken up from the spirometer, now it became a horizontal line, and the respiratory curve of the opposite lung dropped at a more rapid rate, indicating that more oxygen was being absorbed by the lung through which the total circulation was passing. After an interval of fifteen minutes all the studies were repeated. Then the animal was killed by injecting a saturated solution of magnesium sulphate into either the femoral artery or the jugular vein. Immediate necropsy was performed to determine especially the presence of atelectasis and the position of the cannula in the left bronchus. Before opening the thorax the outlets of the cannula were clamped to prevent collapse of the lungs.

RESULTS

Twelve experiments were completed successfully. The primary branch of the right pulmonary artery was occluded in six of these and that of the left in the other six. Measurements of cardiac output were made in all the experiments. In eleven of them additional measurements were made of tidal air and the minute volume of pulmonary ventilation. This was impossible in one experiment (No. 92) because of rapid and irregular breathing. A summary of the experimental results is presented in Tables I and II.

1. *Changes in Cardiac Output.* The changes in cardiac output which were observed after occlusion of the *left* pulmonary artery were in-

TABLE I

EFFECT OF OCCLUDING LEFT BRANCH OF PULMONARY ARTERY

SUMMARY OF EXPERIMENTAL DATA		EXPERIMENT 69 OCT. 14, 1932 WEIGHT, 12.2 KG. MALE BARB. SOD. 3.7 GM.		EXPERIMENT 70 OCT. 21, 1932 WEIGHT, 10.0 KG. FEMALE BARB. SOD. 2.5 GM.		EXPERIMENT 72 NOV. 4, 1932 WEIGHT, 14.1 KG. FEMALE BARB. SOD. 4.0 GM.		EXPERIMENT 81 JAN. 31, 1933 WEIGHT, 16.8 KG. MALE BARB. SOD. 5.0 GM.		EXPERIMENT 88 MAR. 29, 1933 WEIGHT, 19.4 KG. FEMALE BARB. SOD. 5.8 GM.		EXPERIMENT 92 MAY 2, 1933 WEIGHT, 16.1 KG. FEMALE BARB. SOD. 4.8 GM.	
		CONTROL PERIOD	15 MIN. P. OCCL. OF LF. ART.	CONTROL PERIOD	10 MIN. P. OCCL. OF LF. ART.	CONTROL PERIOD	11 MIN. P. OCCL. OF LF. ART.	CONTROL PERIOD	15 MIN. P. OCCL. OF LF. ART.	CONTROL PERIOD	15 MIN. P. OCCL. OF LF. ART.	CONTROL PERIOD	17 MIN. P. OCCL. OF LF. ART.
Oxygen absorbed, c.c. per minute	Total	88.0	90.3	84.0	80.5	82.8	86.3	67.9	71.3	116.5	111.0	75.2	79.4
	By right lung	52.9	90.3	43.7	80.5	47.7	86.3	38.0	71.3	74.8	111.0	44.3	79.4
	By left lung	35.1	00.0	40.3	00.0	35.1	00.0	29.9	00.0	41.7	00.0	30.9	00.0
Oxygen absorbed, per cent	By right lung	60.1	100.0	52.0	100.0	57.6	100.0	56.0	100.0	64.2	100.0	58.9	100.0
	By left lung	39.9	00.0	48.0	00.0	42.4	00.0	44.0	00.0	35.8	00.0	41.1	00.0
Tidal air, c.c. per minute	Total	203	185	72	72	83	91	84	72	130	105	--	--
	Of right lung	97	138	41	48	44	55	44	51	83	69	--	--
	Of left lung	106	47	31	24	39	36	40	21	47	36	--	--
Tidal air, per cent	Of right lung	47.8	74.6	56.9	66.7	53.0	60.4	52.4	70.8	63.8	65.7	--	--
	Of left lung	52.2	25.4	43.1	33.3	47.0	39.6	47.6	29.2	36.2	34.3	--	--
Oxygen capacity		16.3	15.9	16.3	17.2	18.2	19.4	21.4	21.8	22.9	23.3	20.4	20.4
Oxygen content of arterial blood		15.7	15.6	16.7	17.3	18.8	19.4	20.1	21.0	22.6	23.1	19.6	19.1
Oxygen content of venous blood (per cent by volume)		12.6	12.5	12.2	12.7	15.8	16.1	18.2	19.5	19.1	18.1	16.1	15.3
Saturation of arterial blood per cent		96.3	98.1	102.5	100.6	103.3	100.0	94.0	96.3	98.7	99.1	96.1	93.6
Saturation of venous blood per cent		77.3	78.6	74.8	73.2	86.8	83.0	85.0	89.4	83.4	77.7	78.9	75.0
Arteriovenous oxygen difference		3.1	3.1	4.5	4.6	3.0	3.3	1.9	1.5	3.5	5.0	3.5	3.8
Cardiac output, c.c. per minute		2839	2913	1867	1750	2760	2615	3574	4753	3329	2220	2149	2089
Through right lung		1707	2913	971	1750	1590	2615	2000	4753	2137	2220	1266	2089
Through left lung		1132	000	896	000	1170	000	1574	000	1192	000	883	000
Respiratory rate		10	13	37	53	50	54	30	47	44	75	--	--
Pulse rate		180	188	176	198	144	158	146	142	154	140	144	142

TABLE II

EFFECT OF OCCLUDING RIGHT BRANCH OF PULMONARY ARTERY

SUMMARY OF EXPERIMENTAL DATA		EXPERIMENT 84 FEB. 21, 1933 WEIGHT, 12.0 KG. FEMALE BARB. SOD. 3.6 GM.		EXPERIMENT 85 FEB. 28, 1933 WEIGHT, 14.9 KG. FEMALE BARB. SOD. 4.5 GM.		EXPERIMENT 86 MARCH 7, 1933 WEIGHT, 17.8 KG. MALE BARB. SOD. 5.3 GM.		EXPERIMENT 89 APRIL 4, 1933 WEIGHT, 14.5 KG. FEMALE BARB. SOD. 4.3 GM.		EXPERIMENT 90 APRIL 11, 1933 WEIGHT, 13.6 KG. FEMALE BARB. SOD. 4.0 GM.		EXPERIMENT 91 APRIL 25, 1933 WEIGHT, 11.9 KG. BARB. SOD. 3.5 GM.	
		CONTROL PERIOD	15 MIN. P. OCCL. OF RT. ART.	CONTROL PERIOD	13 MIN. P. OCCL. OF RT. ART.	CONTROL PERIOD	15 MIN. P. OCCL. OF RT. ART.	CONTROL PERIOD	15 MIN. P. OCCL. OF RT. ART.	CONTROL PERIOD	15 MIN. P. OCCL. OF RT. ART.	CONTROL PERIOD	15 MIN. P. OCCL. OF RT. ART.
Oxygen absorbed, c.c. per minute	Total	47.1	46.2	56.5	56.6	93.4	95.4	96.8	97.3	56.3	54.9	55.0	61.2
	By right lung	27.6	00.0	31.1	00.0	48.9	00.0	61.0	00.0	33.4	00.0	34.5	00.0
	By left lung	19.5	46.2	25.4	56.6	44.5	95.4	35.8	97.3	22.9	54.9	20.5	61.2
Oxygen absorbed, per cent	By right lung	58.6	00.0	55.0	00.0	52.4	00.0	63.0	00.0	59.3	00.0	62.7	00.0
	By left lung	41.4	100.0	45.0	100.0	47.6	100.0	37.0	100.0	40.7	100.0	37.3	100.0
Tidal air, c.c. per minute	Total	111	136	153	199	111	102	77	112	115	138	93	99
	Of right lung	60	58	83	106	64	41	41	62	69	74	60	55
	Of left lung	51	78	70	93	47	61	36	50	46	64	33	44
Tidal air, per cent	Of right lung	54.1	42.6	54.2	53.3	57.7	40.2	53.2	55.4	60	53.6	64.5	55.6
	Of left lung	45.9	57.4	45.8	46.7	42.3	59.8	46.8	44.6	40	46.4	35.5	44.4
Oxygen capacity		19.7	20.4	19.7	20.0	21.5	21.5	24.3	23.8	23.1	23.1	20.4	20.4
Oxygen content of arterial blood		19.6	19.6	19.4	19.4	20.5	20.8	23.5	23.7	23.5	23.3	20.4	20.0
Oxygen content of venous blood (per cent by volume)		15.9	15.7	16.2	17.1	16.0	13.9	17.9	17.0	17.2	18.1	18.3	17.6
Saturation of arterial blood per cent		99.5	96.1	98.4	97.0	95.3	96.7	96.7	99.6	101.7	100.9	100.0	98.0
Saturation of venous blood per cent		80.7	77.0	82.2	85.5	74.4	66.8	73.7	71.4	74.5	78.3	89.7	86.2
Arteriovenous oxygen difference		3.7	3.9	3.2	2.3	4.5	6.9	5.6	6.7	6.3	5.2	2.1	2.4
Cardiac output, c.c. per minute		1273	1185	1766	2461	2076	1383	1728	1452	894	1056	2619	2550
Through right lung		746	000	972	000	1087	000	1089	000	530	000	1643	000
Through left lung		527	1185	794	2461	989	1383	639	1452	364	1056	976	2550
Respiratory rate		11	8	6	5	29	33	43	53	14	19	34	53
Pulse rate		126	116	115	112	178	160	150	158	142	150	142	135

significant in four experiments (Nos. 69, 70, 72, and 92). In one (experiment No. 81), cardiac output increased 33.1 per cent, and in another (experiment No. 88) it decreased 33.3 per cent.

Changes in cardiac output after occlusion of the *right* pulmonary artery were less constant. They were insignificant only twice (experiments Nos. 84 and 91). In two other instances (experiments Nos. 90 and 85) there were increases of 19.1 and 39 per cent, and in the remaining two (experiments Nos. 86 and 89) the output decreased 33.7 and 16.2 per cent.

The factors or influences which operated in some experiments to increase cardiac output and in others to decrease it were not discovered.

2. *Changes in Tidal Air.* After occlusion of the *left* pulmonary artery the ratio of the tidal air of the left lung to that of the right decreased in every instance. Of the six experiments the changes were significant in five (Nos. 69, 70, 72, 81, and 92); in one (No. 88) they were slight. The actual amounts of air moved by the left lung likewise decreased in every instance, but the decrease in one experiment (No. 72) was insignificant. This decrease in the tidal air of the left lung was accompanied by an increase in the tidal air of the right lung four out of five times. Total tidal air decreased three times (experiments Nos. 69, 81, and 88), increased once (experiment No. 72) and in the other experiment (No. 70) did not change.

Changes in the ratio of the tidal air of the right lung to that of the left after occlusion of the *right* pulmonary artery were similar to those observed after occlusion of the left in four of the six experiments (Nos. 84, 86, 90, and 91), that is, the percentage of tidal air moved by the lung with the occluded blood supply (this time the right) decreased, whereas the percentage moved by the opposite lung increased. In the other two experiments (Nos. 85 and 89) the variations were not sufficiently great to be of significance. Whereas the actual amounts of air moved by the left lung decreased significantly five out of six times when its blood supply was interrupted, a significant decrease in the amount of air moved by the right lung, when its artery was occluded, was observed only once (experiment No. 86). In three experiments (Nos. 84, 90, and 91) the changes were inconsequential, and in two (Nos. 85 and 89) the tidal air increased. The tidal air of the opposite lung (the left), through which the total circulation was shunted, increased significantly in every experiment, a change similar to that which was observed in the right lung four out of five times after occlusion of the left artery.

Changes in total tidal air after occlusion of the right artery were more constant than those observed after occlusion of the left. In five of six instances the total tidal air increased.

3. *Changes in the Functional Residual Air.** When either primary branch of the pulmonary artery is suddenly occluded, the respiratory tracing of the corresponding lung (representing rate of oxygen absorption) does not become horizontal immediately. Instead there is a brief period during which the slope of the curve is reversed, indicating an increase in the volume of gas in the spirometer and a corresponding decrease in the volume of gas in the lung (decrease in functional residual

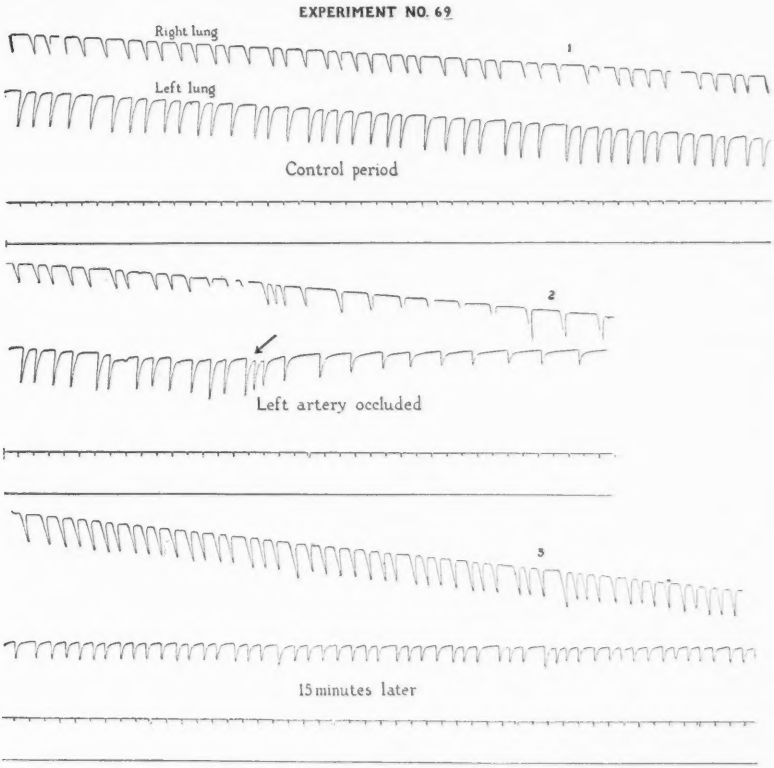

Fig. 3.—The effect of sudden occlusion of the left primary branch of the pulmonary artery. The reversal of the slope of the oxygen absorption curve of the left lung which occurred immediately after the artery was occluded is shown in period 2. In the third period the respiratory tracing of the "occluded" lung is horizontal and the ratio of the depth of breathing of the "occluded" lung to that of the opposite lung is noticeably less than it was in the control period. Time interval, five seconds.

air). Then the tracing becomes horizontal and remains so as long as occlusion of the artery is maintained (Figs. 3 and 4).

4. *Changes in Respiratory Rate.* In nine out of twelve instances the respiratory rate increased; in two it decreased, and in one it could not

*The functional residual air is the amount of air remaining in the lung after a normal expiration (Christie, R. V.: The Lung Volume and Its Subdivisions, 1. Methods of Measurement, J. Clin. Investigation **11**: 1099, 1932).

be measured because of irregularity of the tracing. Similar variations in the magnitude of increase occurred in both series.

5. *Changes in Minute Volume of Pulmonary Ventilation.* The total minute volume of pulmonary ventilation (tidal air multiplied by respira-

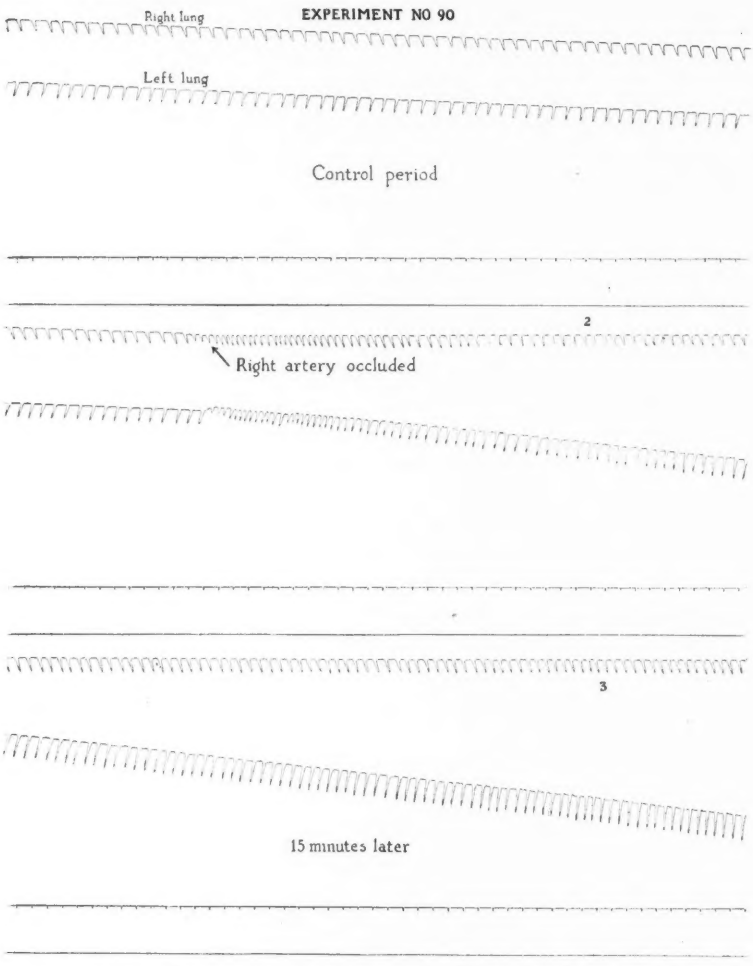

Fig. 4.—The effect of sudden occlusion of the right primary branch of the pulmonary artery. See legend for Fig. 3.

tory rate) increased in eleven of the twelve experiments. The respiratory minute volume of the lung with unoccluded artery, i.e., the lung through which the total circulation was shunted, increased in every instance. Changes in the respiratory minute volume of the lung with oc-

cluded artery were variable. When the left artery was occluded, the ventilation of the left lung decreased three times (experiments Nos. 69, 81, and 72) and increased twice (experiments Nos. 70 and 88). Following occlusion of the right artery the ventilation of the right lung decreased twice (experiments Nos. 84 and 86) and increased four times (experiments Nos. 85, 89, 90, and 91).

6. *Changes in Oxygen Absorption and Oxygen Saturation of Arterial Blood.* When the function of a lung is completely destroyed, as it was in these experiments, it is necessary that the rate at which oxygen is absorbed by the opposite lung increase if oxygen requirements are to be maintained and anoxemia avoided. The "opposite" lung readily assumed the full burden of external respiration in all our experiments, and the variations in the oxygen saturation of the arterial blood after exclusion of the vascular area of one entire lung were not significant.

7. *Observations Made at Necropsy.* In a few experiments the lung through which the total circulation was shunted, and whose tidal air and minute volume of ventilation increased, appeared to contain more air, was paler and presented a smoother surface than the "occluded" lung. In most of the experiments, however, there was no appreciable difference in the appearance or consistency of the two organs. Small confluent areas of atelectasis were usually found in the lung tissue immediately adjacent to the left hilus. These were attributed to operative trauma.

DISCUSSION

The *changes in cardiac output* which followed sudden occlusion of one of the main branches of the pulmonary artery differed from those which followed occlusion of a primary bronchus with complete collapse of the corresponding lung; in the latter instance a marked decrease in cardiac output occurred in more than 90 per cent of the experiments, while in the former no significant change was observed in half of the experiments, and in the other half moderate increases in three cases were balanced by comparable decreases in three others. Also occlusion of the right pulmonary artery produced no changes in cardiac output characteristically different from those produced by occlusion of the left. It seems to be a fact, therefore, that the total circulation can be shunted through either lung without any significant change in cardiac output; and indeed it would seem from our experience that this was usually the case. Our observations agree with those which were made by Tigerstedt,[11] Underhill,[13] and Haggart and Walker[14] after ligation of the left branch of the pulmonary artery. Measurements were made with a Stromuhr by Tigerstedt and with cardiometers by Underhill and Haggart and Walker. On the other hand, Drinker, Churchill and Ferry[26] found that occlusion of the right branch of the pulmonary artery in a heart-lung preparation in the cat was followed immediately by a decrease in aortic output.

And both Haggart and Walker[14] and Gibbon, Hopkinson and Churchill[35] showed that when the main stem of the pulmonary artery was partially occluded circulatory collapse occurred when about 60 per cent of the artery was blocked. We believe that our experiments are an improvement over those of the above mentioned investigators because they were performed on intact animals, and because cardiac output was estimated by the Fick principle rather than from tracings made by cardiometers.

Our previous studies have shown that in the dog the fractions of blood passing through the right and left lungs are approximately in the ratio of three to two. Consequently, when the left branch of the pulmonary artery is occluded and there is no resulting change in cardiac output, the amount of blood passing through the right lung is increased by 66⅔ per cent, whereas the increase in the amount of blood passing through the left lung after occlusion of the right branch of the pulmonary artery is 150 per cent. When the shunting of blood through one lung is followed by an increase in cardiac output, as was sometimes the case, the percentage changes were, of course, even more marked.

If a primary branch of the pulmonary artery can be ligated without any appreciable effect on cardiac output, one would not expect such an occlusion to be associated with any change in systemic blood pressure. We did not study this point, but previous observers have found that it is true.* On the other hand, immediate increases in blood pressure in the main stem of the pulmonary artery have been constantly observed after ligation of the left branch.† In this connection it is of interest that in Graham's and Singer's case[39] sudden obstruction of the pulmonary artery was not followed by any of the signs or symptoms of pulmonary embolism.

The *changes in the ventilation* of a lung which accompany changes in the minute volume of blood passing through it are of particular interest and can be interpreted as demonstrating a direct relation between circulation and expansion. Two of the observations which were made tend to show this: (1) *the decrease in the percentage of tidal air moved by either lung after occlusion of its artery, and* (2) *the immediate transitory reversal of the slope of the oxygen absorption tracing of the occluded lung before it became horizontal.*

*In 1876 Lichtheim[7] published a report of a series of experiments in which he stated that ligation of the left branch of the pulmonary artery in rabbits and dogs under the conditions of artificial respiration has no influence on the arterial blood pressure. Although Landgraf[6] was unable to confirm Lichtheim's results in rabbits that breathed spontaneously, ligation of the left pulmonary artery without any accompanying decrease in arterial pressure in free breathing animals has since been observed by Gerhardt,[8] Plumier,[9] and Haggart and Walker.[14] Similar observations were made by Kuno[12] with the heart-lung preparation and by Tigerstedt,[10, 11] and Underhill[13] in animals that were artificially ventilated.

†Landgraf[6] reported distention of the pulmonary artery and swelling and dilatation of the right heart after ligation of the left primary branch in rabbits, and immediate increases in pulmonary pressure were observed by Kuno,[12] Underhill,[13] Haggart and Walker,[14] and Scarff.[15]

The decrease in the percentage of the tidal air moved by one lung after occlusion of its pulmonary artery, and the corresponding increase in the percentage of the tidal air moved by the contralateral lung through which the total circulation is shunted, suggest that the pressure in the pulmonary vascular bed resists the elastic recoil of the lung and in this way aids expansion. It is reasonable to assume that the pressure in the vascular bed of a lung whose pulmonary artery has been occluded is zero, and an increase of pressure in the main stem of the pulmonary artery after occlusion of one of its primary branches has been repeatedly demonstrated (see above). Since the pressure of the blood delivered to the lung with unoccluded artery is increased, it is also reasonable to assume that the pressure in the vascular bed of that lung is increased. It is impossible to say from the evidence which we have whether the percentage changes in the tidal air of the two lungs occur simultaneously or whether the increased expansion of the lung through which a larger volume of blood is passing at an increased pressure is secondary to a contraction of the occluded lung, or vice versa. However, it can definitely be stated that when the circulation through one lung is completely interrupted and the circulation through the opposite is greatly increased, without any disturbance in the respiratory mechanism, the percentage of tidal air (expansion) moved by the former decreases, whereas that moved by the latter increases.

This is in contrast to the findings of Churchill and Agassiz.[16] These authors, working with cats prepared according to the Drinker method, found no significant change in the relative volumes of air moved by the two lungs within an hour after occlusion of the right branch of the pulmonary artery. On the other hand, Churchill and Agassiz found that in certain instances, at the end of an hour, the lung with unoccluded artery moved relatively more air. Their additional finding that there is an immediate increase in the total minute volume of ventilation after occlusion of the right branch of the pulmonary artery is confirmed by our results. In subsequent experiences with the same preparation Churchill[17] found that the respiratory minute volume of the left lung increased thirteen out of fifteen times after occlusion of the right branch of the pulmonary artery. We have confirmed this observation and also observed constant increases in the respiratory minute volume of the right lung after occlusion of the left branch of the pulmonary artery.

In a later paper Churchill[18] states that the increase in the total minute volume of ventilation which follows occlusion of the right branch of the pulmonary artery is shared equally by the two lungs, but that when the left pulmonary artery is occluded the response is a decrease in the minute volume of ventilation of the left lung and an increase in that of the right. Our results differed from these in that the changes in the respiratory minute volume of the lung with occluded artery were less constant

After occlusion of the right artery we observed an increase only four out of six times, and after occlusion of the left artery there was a significant decrease in only two of the five experiments in which the measurement was made. Furthermore, we found, in contrast to Churchill, that the increase in total ventilation after occlusion of the right artery usually was not shared equally by the two lungs. In two of our six experiments the minute ventilation of the right lung decreased and in the others increases were much less than they were in the opposite lung.

The other observation made by us, which we feel can be justly accepted as evidence that the circulation through the lungs has an influence on the degree of inflation, was the transitory reversal of the slope of the oxygen absorption curve which immediately followed occlusion of the pulmonary artery of either lung. This indicated an increase in the volume of gas in the spirometer and a corresponding decrease in the functional residual air of the lung. It is generally considered that the degree of expansion of a lung is dependent upon an equilibrium between the elastic recoil of that lung and the negative intrathoracic pressure. Since nothing was done to change either of these factors in our experiments, the observed decrease in the functional residual air of the "occluded" lung can be interpreted as indicating another factor opposing the elastic recoil of the lung. This factor is presumably the pressure in its vascular bed. Whether the decrease in the functional residual air of the "occluded" lung is due to contraction of the lung which follows obliteration of the pressure in its vascular bed or to compression which follows an increase in the volume (functional residual air) of the opposite lung because of the increased pressure in its vascular bed is beside the point. Presumably both phenomena take place.*

Several authors have previously touched on this subject. In 1923, Yates[36] advanced the hypothesis that when increased amounts of blood are delivered to parts of a lung, there is a corresponding increase in the degree of inflation of those parts. In 1925[37] he developed this theory and attempted to explain the origin of compensatory emphysema in this way. Graham,[38] in his discussion of Yates' second paper, refuted the theory, assuming that the capillaries receiving increased amounts of blood are distended and stating that distention of pulmonary capillaries causes a decrease rather than an increase of pulmonary inflation. Since an increase in the circulation through a part of a lung does not necessarily imply distention of the capillaries, it would seem that there was

*A change in the slope of the oxygen absorption curve of the "unoccluded" lung, occurring simultaneously with the shunting of the total circulation through it, and indicating an increase in its volume was not observed. We do not believe, however, that our apparatus was sensitive enough to record such a change. Since the slope of the "unoccluded" lung naturally becomes steeper at this time, the added effect of a slight additional change in the same direction could hardly be expected to be apparent in the tracing.

no fundamental conflict between the two views. Our observations support Yates' hypothesis in that they seem to show an immediate decrease in the inflation of a lung when its circulation is removed.

SUMMARY

The effects of sudden occlusion of either primary branch of the pulmonary artery on cardiac output and the expansion of each lung were studied in twelve anesthetized dogs. The method used made it possible to occlude the artery in an animal breathing naturally with chest closed, and the preparation consisted of two separate respiratory units, each of which was connected with a lung through one barrel of a double cannula. From the tracings so obtained the tidal air and rate of oxygen absorption of each lung were calculated. The oxygen contents of arterial and mixed venous blood samples, taken while the respiratory curves were being recorded, were estimated by the Van Slyke and Neill manometric method, and cardiac output was calculated according to the Fick principle. Measurements of cardiac output and pulmonary ventilation made fifteeen minutes after occlusion of the artery were compared with control studies made on the same preparation immediately before the artery was occluded. It was found that:

1. The changes in cardiac output were insignificant in half of the experiments and varied in the other half as much in one direction as in the other. There was less variation after occlusion of the left branch than there was after occlusion of the right.

2. The ratio of the tidal air of the "occluded" lung to that of the other decreased in ten experiments. In the remaining two the changes were not sufficiently great to be of significance. The changes in the actual amounts of air moved were less constant.

3. There was an immediate small decrease in the volume of air in either lung after its artery was occluded.

CONCLUSIONS

1. The total circulation can be shunted through either lung in anesthetized dogs without any significant change in cardiac output.

2. The decrease in cardiac output which has been observed after complete occlusion of one primary bronchus is not due to resistance to the passage of blood through the atelectatic lung.

3. The expansion of a lung is affected by its pulmonary circulation, decreasing when the pulmonary circulation is interrupted and increasing when the pulmonary circulation is increased.

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SURGICAL TREATMENT IN FOURTEEN CASES OF MEDIASTINAL OR INTRATHORACIC PERINEURIAL FIBROBLASTOMA*

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A RELATIVELY high percentage of tumors arising within the thorax, particularly those in the posterior mediastinum, originate from the thoracic spinal root nerves and along the course of the intercostal nerves. In my experience with forty-six intrathoracic tumors removed at operation, eleven of them proved, on microscopic examination, to be neurofibromas, ten of which were situated in the posterior mediastinum and one in the left wall of the thorax, along the course of the ninth intercostal nerve; two were cellular fibromas situated in the posterior mediastinum, and one was a fibromyxosarcoma situated in the posterior mediastinum. Inasmuch as all of these tumors are thought to be derived from the sheaths of the nerves, I have grouped them under the one term "perineurial fibroblastoma." Thirteen of the growths were benign, and one was malignant.

The purpose of this paper is to give a brief summary of the clinical symptoms, surgical treatment, and results of operation in these fourteen cases. Nine of the cases previously have been reported in detail, and only reference will be given in regard to them. In four cases, the complete histories will be given at this time, and the remaining case, in which there was a dumb-bell type of neurofibroma, will be reported subsequently, as an individual case report, by Dr. W. McK. Craig and me.

This group of tumors is of particular interest because of the relatively high percentage of growths which are found to be benign. The older view was that most tumors occurring in the mediastinum were malignant. This was probably due to a study of material obtained at necropsy of subjects who had succumbed to the disease, which had been of long standing, and in whose cases the growths had become malignant. I believe that the high percentage of benign growths in this series is due to early removal, before the growth has undergone malignant change. This has been made possible by the marked advance in the methods of thoracic diagnosis, and to improved surgical technical methods of removing intrathoracic lesions, in recent years.

The establishment of a definite clinical diagnosis often is difficult, but a diagnosis usually can be established by correlation of the clinical symp-

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toms, physical findings, and results of roentgenologic examination. The last is the most important of all diagnostic methods. Thoracoscopic and bronchoscopic examinations are also often of diagnostic value in selected cases.

CLINICAL SYMPTOMS

Study of the clinical symptoms in these cases is of practical importance. I believe that the outstanding subjective features are the relatively few and mild symptoms which are associated with such large intrathoracic growths. This is particularly true in cases of benign tumor. When these growths undergo malignant change, the symptoms become very severe, particularly the pain, which is the most important subjective symptom in distinguishing benign from malignant growths. The pain of malignant lesions becomes very marked, usually more severe at night, and often requires sedatives for relief. The other symptoms associated with malignant lesions are due to infiltration of the malignant growth, and in one case of this group the patient presented a Horner's syndrome and infiltrating destruction of the overlying ribs. Pain was present in eight of the cases in this series in which the growth was benign. It was usually of a dull, aching type, more demonstrable on exertion, and often followed the course of the intercostal nerves. This pain did not seem to have any direct relation to the size of the tumor but was more dependent on the situation of the growth. Tumors in the upper part of the mediastinum present more symptoms of pain than those in the lower part of the mediastinum. It is of interest to note that in five cases pain was not associated with the tumor; in one of these cases the tumor was the largest of the entire series, weighing 825 gm. and measuring 14 by 13 by 8 cm. This tumor presented in the lower left portion of the thorax, and even though it was pressing against the pericardium, the patient had no subjective symptoms.

The most common symptom in this group of cases was dyspnea, and the chief complaint was of dyspnea in most cases. It was present in nine cases of this series, and had a direct relationship to the size of the tumor and also to its situation. Those tumors situated in the upper part of the thorax uniformly caused symptoms of dyspnea. This was probably due to pressure on the trachea as well as to interference of expansion of the lung, the result of the size of the growth. In one case, the dyspnea was due to a bloody pleural effusion. This is of interest because the patient's age was sixty years, and the condition was thought to be malignant, clinically. The tumor proved to be benign. It is the only case in my experience in which a benign tumor was associated with bloody pleural effusion.

Cough was noted in three cases. This was an irritative type of cough and often was associated with mucoid expectoration. Cough was present

in those cases in which the tumor was situated in the upper part of the mediastinum and thorax, and probably was due to tracheal irritation.

Dysphagia was present in three cases. In all of these cases there was marked pressure on the esophagus, which could be demonstrated by roentgenologic examination after introduction of barium into the esophagus, which gave evidence of definite deformity and partial obstruction of the lumen of the esophagus.

Loss of weight was present in three cases. In one of these the tumor was malignant. However, the loss was only 5 pounds (2.3 kg.) over a period of a year and a half; in two cases of benign tumor loss of weight was, respectively, 5 pounds and 20 pounds (9 kg.); this loss I did not attribute to the tumor, but to other associated conditions.

It is interesting to note that symptoms of chronic nervous exhaustion and fatigue were present in six cases. In four of these cases there was associated secondary anemia. Whether or not the presence of the tumor had any bearing on these symptoms is problematical, for the tumors were all benign, and it is likely that these were associated symptoms and not due to the tumor.

The chief complaint in one case was spells of smothering. These were due to cardiac disease, and had no direct relation to the presence of the tumor in the mediastinum, which was relatively small in size and was benign.

Neurologic symptoms were present in two cases of the entire group. In one case a malignant tumor was found high in the posterior mediastinum, and the patient presented a Horner's syndrome from involvement of the inferior cervical sympathetic ganglion as well as pain extending down the ulnar distribution of the right arm, probably resulting from involvement of the cervical root nerves. This case is of particular interest because it is the only case of the entire series in which the growth was malignant, and the patient had had pain extending down the arm, of twenty-four years' duration. The pain had started when the patient was seven years of age. As a child, these symptoms had been treated as those of neuritis. The tumor had been found accidentally, four years before the patient's admission to the clinic; no significance had been attached to it or to the pain in the arm until three and a half years later, when the same type of pain became more constant and severe, requiring sedatives for relief. These symptoms indicate that the tumor had primarily been benign and had undergone malignant change. Symptoms referable to the spinal cord were present in one case of a dumb-bell type of tumor. The growth was situated both in the spinal cord and in the posterior mediastinum. The patient's chief complaint was weakness in the knees, and incoordination of the movements of the left leg, associated with attacks of staggering which had been present during the last year.

The duration of symptoms in these cases was from one to twenty-four years, with an average of more than four years, which indicates that these tumors are present over a long period of time before they produce symptoms of sufficient severity for the patient to seek relief. In four cases, the tumor was found accidentally in the course of examination for some other condition, and the growth had not produced symptoms sufficient to indicate its presence. In three cases the symptoms had been augmented during the last month, due to recent increase in size of the growth.

There seems to be no definite age incidence for the occurrence of these tumors. The ages of the patients in the benign cases, in years, were twenty-two, twenty-five, twenty-seven, thirty-four, thirty-five, thirty-five, thirty-eight, forty-five, forty-six, forty-eight, fifty-three, fifty-five, and sixty. In the one case of malignant growth, the age of the patient was thirty-one years. This patient presented subjective symptoms over a period of twenty-four years.

Physical examination is of importance only in determining the presence of the tumor, and does not give definite knowledge as to the type of tumor which is present. In one case of this series, in which the tumor was in the lateral wall of the thorax, there was a bulging of the chest wall at the site of the tumor, and in the other thirteen cases, in which the tumors were in the posterior mediastinum, there was no external evidence of the presence of the tumor within the thorax. In all of these cases, the physical findings of a solid tumor were elicited by percussion and auscultation. In those cases in which the symptoms are very mild, these physical findings are of importance, for they indicate the necessity of special thoracic examination.

Roentgenologic examination of the thorax is of paramount importance in establishing a diagnosis. As has been noted in four of these cases, the tumor was found accidentally in the course of general examination, which included roentgenologic examination of the thorax. Roentgenograms should be taken in the anteroposterior, true lateral, and oblique positions; stereoscopic roentgenograms, and fluoroscopic examination of the thorax, are of great value in determining the true position of the growth and its relation to the surrounding normal structures of the thorax. The value of roentgenologic studies is often greatly enhanced by induction of artificial pneumothorax before the examination, but artificial pneumothorax is often impossible in these cases because of adhesions between the visceral and parietal pleura surrounding the tumor. The more common roentgenologic sign presented by these tumors is that of a circumscribed shadow, rounded in contour, presenting a sharp border, and situated in the posterior mediastinum. In some instances these tumors produce pressure erosion of the adjacent ribs, and in those cases in which the tumors arise within the spinal cord or inter-

vertebral foramina, they present a very definite roentgenologic picture, as has been described by Camp. The early changes within the cord produce pressure, and erosion and thinning of the mesial border of one or more pedicles of the vertebra at the site of the tumor. Later there is evidence of erosion and thinning of the lamina, and if the tumor attains sufficient size, it may produce changes in the bodies of the adjacent vertebrae. When the tumor extrudes through the intervertebral foramen, there is pressure-erosion of the adjacent bony structures, producing marked enlargement of the intervertebral foramen. As the tumor enlarges in the posterior mediastinum, sufficient pressure may be exerted to produce widening of the intercostal spaces and erosion of the adjacent ribs. All these changes were noted in one case of this series, that of a dumb-bell-shaped neurofibroma of the spinal cord and posterior mediastinum. Pressure-erosion of the ribs was present in two cases; in one case in which a neurofibroma evidently had originated just outside of the intervertebral foramen, and in the one case in which the tumor was malignant, and of long standing. In the majority of cases in this series, changes were not demonstrable in the ribs, by roentgenologic examination, to assist in establishment of the diagnosis. In these cases, there were only large, rounded tumors in the posterior mediastinum, which, on fluoroscopic examination, were seen to be not pulsating. The growths in earlier cases of this series, in which this appearance was presented were thought to be malignant tumors roentgenologically, because of the similarity to the roentgenologic findings in the presence of tumors from the bone and spine in this region, which are usually sarcomas. These tumors, however, are associated with an infiltrative type of destruction to the adjacent bone, and clinically give many more subjective symptoms of pain. Injecting the bronchial tree with lipiodol, and bronchoscopic examination, are often of value in distinguishing between an intrapulmonary and an extrapulmonary lesion.

In my experience the lesions most to be considered in differential diagnosis, have been aneurysm of the arch of or descending portion of the aorta, sarcoma originating from the vertebrae or ribs, and endothelioma. The aneurysm usually can be distinguished by physical examination and fluoroscopic examination of the thorax. The malignancy of the bone usually can be identified by roentgenologic examination of the chest, as well as by clinical subjective symptoms, of which pain is the most conspicuous. In the one case of endothelioma in the posterior mediastinum, which I have seen, the condition was not identified by roentgenologic methods or by clinical findings, and the growth was diagnosed preoperatively as a neurofibroma.

As can be seen by the foregoing, it may be impossible to establish a definite clinical diagnosis, with utilization of all the armamentarium of thoracic diagnosis. In some instances, the diagnosis can be estab-

lished by thoracoscopic examination, with removal of a specimen from the tumor, but in most instances in which there is a sufficient indication to justify the use of a thoracoscope, I prefer to do exploratory thoracotomy, for in many instances adhesions will prevent use of the thoracoscope, and the additional knowledge that can be gained by thoracotomy justifies any additional risk that is produced by the operative procedure.

SURGICAL TREATMENT

The most important consideration in surgical treatment of these lesions is early removal before they have undergone malignant change. The immediate operative risk is often decreased by preliminary induction of artificial pneumothorax, which permits the patient to become accustomed to unilateral alteration of pulmonary pressure. This procedure cannot be carried out in all cases, for many of the larger tumors are firmly adherent to the lung, preventing its collapse by air pressure. When early removal can be accomplished, it should be done from three to five days before operation. A thorough general examination is of importance, particularly in regard to the condition of the heart, for any cardiac lesion greatly increases the hazard of intrapulmonary operations.

The chief surgical technical problems are those associated with the method of approach through the thoracic cage. These include the danger of injury to the structures within the thorax to which the tumor is adherent; the danger of open pneumothorax, and reconstruction of the thoracic cage.

The methods of approach and types of operative procedure depend to some extent on the site of the tumor and the structures to which it may be adherent within the thorax. Each case must be considered individually, depending on the indications presenting. A few general principles can be applied in all cases. The most important are early operation and complete removal of the tumor. The tumor always should be removed by an operation in one stage if possible. In all cases of this series, the tumor was removed in one stage. An attempt always should be made to remove the tumor extrapleurally. This, however, can be accomplished only in a small percentage of cases, for the tumor usually is adherent to the parietal pleura, which is ultimately opened, and in some instances the tumor is placed so far back in the mediastinum that it is impossible to dissect the pleura away from the thoracic wall sufficiently to permit removal of the tumor. In this series of fourteen cases, two tumors were removed by extrapleural operation and twelve by transpleural operation.

The situation of the incision into the thoracic cavity depends on the situation of the tumor. In all cases in which the tumor is situated in the posterior mediastinum, approach through the posterior thoracic wall is indicated. The incision is placed over the site of the tumor, and in

those cases in which the growth is in the posterior mediastinum a posterolateral incision is made around the vertebral border of the scapula. The entrance into the thoracic cavity is made by partial resection of one rib, over the most central portion of the tumor. The thoracic cavity is then opened by incising through the posterior periosteum and pleura of this rib bed. The tumor and its attachments in the pleural cavity are then explored, and if further exposure is desired, it can be accomplished by partial resection of an adjacent rib. In some cases in which there is a small or a collapsible cystic tumor, the growth may be removed through this small opening. If a larger opening is required, for a large, solid tumor, the bordering ribs, both above and below the resected rib, are cut and drilled, and at completion of the operation the cut ends are sutured together to reestablish the contour of the thoracic wall. In this series, three of the tumors were removed by partial resection of two ribs. In ten cases, one rib was partially resected, and from two to four ribs were sectioned and drilled and resutured during the closure. In one case, the tumor was in the lateral thoracic wall. The incision was made over the site of the tumor, and four ribs were partially resected to accomplish complete removal of the tumor. The defect in the thoracic wall was closed with the overlying muscles and soft tissues.

Extreme care should be taken not to injure the structures to which the tumor is adherent within the thorax. There is always a fairly definite capsule over the tumor, which consists of pleura and a thin capsule of the nerve sheath. This capsule contains many large vessels if the tumor is large. By careful dissection, this capsule usually can be separated from the adherent lung without producing any great injury to the lung. In some of the cases in which large tumors are very adherent to the lung, it is necessary to dissect the lung away from the tumor, and careful hemostasis involving attention to the vessels on the surface of the lung is required. Posteriorly, these tumors are often very adherent around the aorta, particularly on the left side, and great care should be exercised not to injure the wall of the aorta. Also, care must be exercised to ligate the intercostal vessels that may be severed in the course of removal of the tumor. It is important to leave in place the posterior portion of the capsule of the tumor, to cover over the raw surface which is left in the parietal pleura after the tumor has been removed. The greatest difficulty in hemostasis is often encountered posteriorly, in dealing with intercostal vessels. In some cases in which there has been some erosion of an intervertebral foramen, hemorrhage may occur from dilated vessels in the spinal cord. This occurred in one case of this series and subsequent laminectomy was required. In one case, a dumb-bell-shaped tumor was removed by laminectomy and posterior mediastinotomy, which were performed at the same time. This case was

encountered recently and is the one, mentioned earlier in the paper, which will be reported in detail at some future time by Dr. Craig and me.

The danger of open pneumothorax, with pulmonary collapse and mediastinal flutter, has been overcome by the use of intratracheal anesthesia induced by means of apparatus by which anesthetic gas and oxygen are administered under positive pressure. Ethylene or acetylene gas was used in all cases. Administration of the anesthetic should be in the hands of a skilled anesthetist. In cases in which partial collapse of the lung is required, the lung should be permitted to expand fully every four or five minutes during the course of the operation. A suction pump should be applied to the intratracheal catheter before it is withdrawn, to remove any mucus which may have accumulated in the trachea.

The thoracic cage should be completely reconstructed, and in cases in which the ribs have been drilled and cut they should be sutured together with catgut. The ribs are cut, back of the erector spinae muscle so that the suture line in the pleura, which is parallel with the vertebral column, can be securely closed, preventing leakage of air. The horizontal incision in the posterior periosteum of the resected rib is closed with continuous sutures of catgut. The lung is fully inflated by use of the positive pressure gas machine, and at the same time the air is aspirated from the pleural cavity just before the last suture is placed, in closure of the pleura. The pleural cavity is usually completely closed without drainage, and this was done in all of the transpleural operations of this series and in one of the extrapleural operations. In the remaining extrapleural operation, which was associated with laminectomy, a soft rubber drain was left in the mediastinum for forty-eight hours, to protect against any accumulation of serum which might cause back pressure on the spinal cord, through the enlarged intervertebral foramen.

Postoperative care is of the utmost importance. Particular care should be taken to maintain the blood pressure and to relieve any respiratory difficulty. It is usually advisable to give some form of medication intravenously, either during the operation or immediately afterward. If there has been much loss of blood, transfusion of blood should be given; if this is not practicable, infusion of acacia is satisfactory. Respiratory difficulty is the most serious immediate complication, and is best relieved by placing the patient in an oxygen cabinet. This is often a life-saving procedure, for sufficient oxygen can be obtained to tide the patient over the most critical postoperative period of respiratory embarrassment. In six cases of the series, transfusion of blood was given on the operating table. In twelve cases the patients were placed in the oxygen cabinet, and in two cases they were placed in oxygen tents immediately on leaving the operating room. The period of hospitalization varied from eighteen days to five and a half months.

Pleural effusion after operation occurred in twelve cases of this series, and required in each of these twelve cases one or more aspirations. In four of the cases encapsulated empyema developed, requiring drainage by resection of a rib. Postoperative hemorrhage into the spinal cord occurred in one case, and laminectomy was necessary subsequently.

Twelve patients recovered from the operation. There were two operative deaths: one on the third day, from cardiac failure and myocardial degeneration, and one on the sixth day, from bronchopneumonia and congenital heart disease. There was one death two and a half years after operation, from recurring malignancy. This was the only case of the entire series in which a malignant growth was present. Eleven patients are living at present, with no recurrence of the tumor, and are completely relieved of symptoms from one year to seven and a half years since operation.

REPORTS OF CASES

CASE 1.—A woman, aged twenty-seven years, consulted physicians of the clinic November 27, 1933, because of dyspnea, cough with slight expectoration, loss of strength, all of about two and a half years' duration. Also, she had had some difficulty in swallowing for the last four months. About two and a half years before her admission to the clinic, an attack of influenza had developed, which had been accompanied by generalized aching, fever, coryza, and nosebleed, cough, and later, abundant foul sputum. She had been confined to bed for about ten days, after which time all symptoms had disappeared, with the exception of weakness. She had felt well throughout the following summer, but with the onset of cold weather she had had frequent colds, cough, slight expectoration, and dyspnea on exertion. One year later, in the autumn, the dyspnea had become more severe, and there had been some "rattling" in her throat. The irritative cough also had returned. With the return of warm weather, in the summer of 1933, the improvement that was usual in summer had not taken place, for the dyspnea had remained severe and the patient had had an occasional cough. In the autumn of 1933, just before her visit to the clinic, the symptoms had become more severe, and she had consulted a physician, who had diagnosed and treated the condition as bronchitis, but without relief. Three weeks before her admission, roentgenologic examination (Fig. 1) had given evidence of a tumor in the right upper part of the thorax. The tumor had been subjected to aspiration, and a considerable amount of bloody, serous fluid had been withdrawn. Since that time, her symptoms had become less marked, although she had continued to be dyspneic on slight exertion, to have an irritative cough, to have slight expectoration and to lack energy. She had noticed a great deal of dyspnea when lying on the right side, but none when lying on the left side. She had not had dysphagia, hemoptysis, or sweating. She had lost about 7 pounds (3.2 kg.) in the last three years.

Physical examination revealed that the woman was well developed. She weighed 118 pounds (53.5 kg.). The systolic blood pressure was 120 mm. of mercury and the diastolic 78 mm. The pulse rate was 80 beats per minute. Slight lymphadenopathy was noted, and both external jugular veins, especially the right, were distorted. The heart was negative to examination. A rounded prominence, posterior to the lower border of the scapula, was evident. Tympany was noted over the left apex, posteriorly, shading off to dullness extending to the angle of the scapula. Over the upper portion of the right lung, bronchial breathing was present, and there were

some bubbling râles shading off to diminished bronchial breathing. There was little change in the right lung anteriorly. The left lung was negative to examination. Urinalysis gave negative results. The value for hemoglobin was 13.7 gm. per 100 c.c. of blood; erythrocytes numbered 4,170,000 and leucocytes 11,400 per cubic millimeter of blood. A flocculation test for syphilis was negative.

A. *B.*

Fig. 1.—(Case 1.) *A*, Large tumor (neurofibroma) filling the entire upper part of the thorax, causing complete collapse of the upper and partial collapse of the middle lobes of the right lung, and also causing marked displacement and partial obstruction of the esophagus. The roentgenogram was taken following introduction of barium into the esophagus; *B*, lateral view, showing the tumor originating in the posterior mediastinum.

Roentgenologic examinations revealed evidence of a large, circumscribed tumor of the upper right portion of the thorax, posteriorly, displacing the esophagus to the left, but not involving the spinal column or ribs. Fluoroscopic examination of the chest disclosed that the tumor was not expansile.

December 2, 1933, under intratracheal ethylene and oxygen anesthesia, the right thoracic cavity was explored. A posterolateral incision was made, extending around

the lower border of the scapula, the posterior halves of the third and fourth ribs were resected, and the parietal pleura was opened by cutting through the posterior periosteum of the resected rib. The large, posterior mediastinal tumor originated from the intercostal space, between the fifth and sixth ribs, at the costovertebral juncture. The tumor was soft, and contained about 500 c.c. of fluid. It was adherent to all surrounding structures and caused marked pressure on the upper and middle lobes of the right lung, to which it was very adherent. The tumor was first separated from the lung, and the bleeding points on the surface of the lung were ligated. It was then separated from the posterior wall of the thorax, at its origin. There was considerable hemorrhage, which was controlled with sutures of catgut. Enough of the capsule of the tumor was left to close over the posterior mediastinal

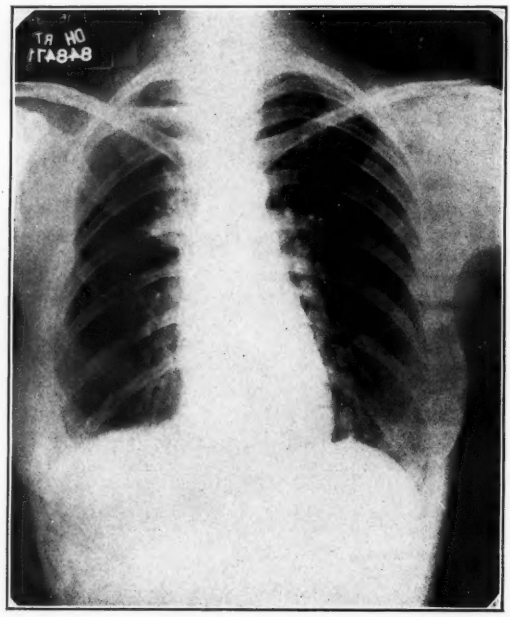

Fig. 2.—(Case 1.) Six weeks after transpleural complete removal of the tumor. Right lung fully expanded.

area from which the tumor had originated. This portion of the capsule was closed with interrupted sutures, leaving a rather smooth surface. The pleural cavity was then washed out with physiologic saline solution, and was closed by suturing the posterior periosteum and pleura in the bed of the fourth rib, without drainage. The posterior thoracic wall was closed in layers, and two Penrose drains were left in place. Transfusion of 500 c.c. of blood was given while the patient was on the operating table, for the blood pressure had gone down to 70 mm. of mercury. Immediately on completion of the operation, the woman was placed in the oxygen chamber. A roentgenogram was made January 15, 1934 (Fig. 2).

The tissue removed was a hemorrhagic, cystic, lipoid, degenerating neurofibroma, weighing 800 gm. and measuring 12 by 12 by 9 cm. (Fig. 3).

Convalescence was uneventful, as far as the thoracic condition was concerned. Three weeks after operation, a very low total leucocyte count developed. The woman

was about to leave the hospital when a temperature of 99.5° F. developed, and she experienced a general feeling of malaise and weakness. It was thought that the slight amount of pleural effusion which had developed postoperatively might have increased, or that the pleural effusion might have become infected; therefore a roentgenogram of the thorax and a leucocyte count were taken. The roentgenogram disclosed that the right lung was practically fully inflated, and that a very slight amount of fluid was present. Leucocytes numbered 1,800 per cubic millimeter of blood, of which 62 per cent were neutrophiles. A possibility of agranulocytosis was

Fig. 3.—(Case 1.) Hemorrhagic, cystic, lipoid degenerating neurofibroma, weighing 800 gm. and measuring 12 by 12 by 9 cm.

suspected, and leucocytes were counted again a few hours later, and were found to number 1,600, 57 per cent of which were neutrophiles. A relatively high proportion of polymorphonuclears and lack of other symptoms ruled out the presence of agranulocytosis. Five days previously leucocytes had numbered 8,800 per cubic millimeter of blood, 80 per cent of which had been neutrophiles. Immediately, bone marrow was given by mouth and response was promptly noted in blood count and clinical symptoms. January 5, 1934, leucocytes numbered 8,200, and the patient's general condition was very much improved. The wound healed by primary union (Fig. 4)

and she was dismissed from the hospital on the forty-eighth day after operation, at which time her lung was fully inflated and her blood was practically normal.

This patient presented the usual subjective symptoms which are associated with large benign tumors in the upper, posterior part of the mediastinum, which are not complicated by pressure on the spinal column and spinal cord. It is difficult to evaluate the relationship between the tumor and the repeated respiratory infections. This association is not usually noted in cases of this type, and it is possible that the disturbed pulmonary ventilation and obstruction produced by the tumor were factors in the frequency of the attacks.

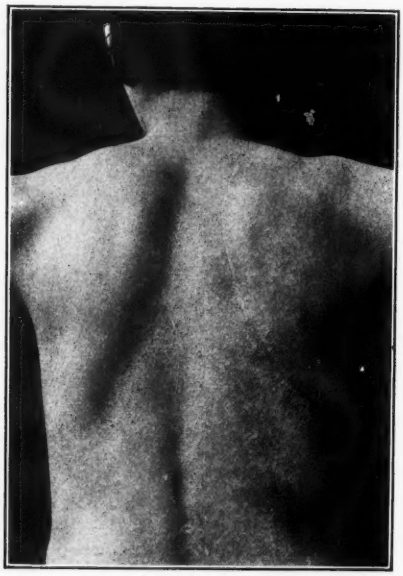

Fig. 4.—(Case 1.) Posterolateral incision entirely healed. No deformity or limitation of motion of arm. Complete relief of symptoms.

Tumors in this region may attain enormous size before they produce symptoms due to pressure on the surrounding structures, particularly the trachea, the spinal structures and the lung. The predominating subjective symptom and chief complaint in this case was dyspnea, which was noted mostly on exertion. This was due both to pressure on the trachea and to the large size of the tumor, which caused complete collapse of the upper and middle lobes of the right lung. The symptoms of esophageal obstruction were of recent onset and were not marked. This was due to the mobility of the esophagus, which permits, as it permitted in this case, considerable distortion before there is enough obstruction to produce symptoms.

The surgical technic in this case was that which I use for tumors of the upper, posterior part of the mediastinum. The approach was made through a posterolateral incision, between the scapula and the spinal column. Because of the deep attachment of the tumor, it was necessary to perform a transpleural type of operation. Because of the cystic character of the tumor, it was possible to remove the growth through a relatively small, intrathoracic opening, after partially resecting two ribs. If the tumor had been solid it would have been necessary to section and cut at least four ribs in order to remove the growth from its situation in the mediastinum. The tumor was extremely vascular, necessitating special care in hemostasis, both in the bed of the tumor in the posterior mediastinum and on the surface of the lung, to which the tumor was very adherent. The importance of careful hemostasis in these cases cannot be overestimated, because there is always a moderate amount of pleural effusion, and when this is complicated by hemorrhage, convalescence is often very seriously complicated.

Convalescence in this case was exceptionally free of complications, as far as the surgical procedure was concerned. Moderate pleural effusion developed, but not to the degree that it required aspiration, and the effusion was gradually absorbed. It was impossible to evaluate the significance of the low leucocyte count in this case, because there was no infection, and it is very possible that had it not been discovered an intercurrent infection might have developed which would have been attributed to the surgical procedure and not to the blood dyscrasia.

CASE 2.—A man, aged twenty-two years, came to the clinic December 15, 1930, because of thoracic pain of three months' duration, due to a tumor in the left thoracic cavity. Evidence of the tumor had been found accidentally, several years before in a roentgenogram of the patient's spinal column, that had been made because of his bad posture. Since then, the man had had periods of paroxysmal cough, coming on in the morning, with expectoration of sticky, gray mucus. He had had his first thoracic pain about three months before his admission. It had become rather troublesome, and had been associated with slight difficulty in moving the left arm. There never had been any blood or hair in the sputum. Slight tenderness had been noted in the left axilla. The left leg had been shorter than the right, and a built-up shoe had been worn for the last eight years.

The patient was 5 feet, 2 inches (157.5 cm.) in height, and weighed 107 pounds (48.5 kg.). The blood pressure was 192 mm. of mercury systolic, and 72 mm. diastolic. The body was sprinkled with dark brown, hairless moles. The heart was enlarged to the left, as far as the anterior axillary line, and a rough systolic murmur was heard over the whole heart, and up into the throbbing carotid arteries. The left leg was smaller than the right, and about 1 inch (2.5 cm.) shorter. The blood pressure in the leg was almost imperceptible. There was a solid tumor of the left upper part of the thorax, with bulging of the left axilla. Urinalysis gave negative results. The value for hemoglobin was 17.2 gm. per 100 c.c. of blood, and leucocytes numbered 12,700 per cubic millimeter of blood. The Wassermann reaction of the blood was negative. The basal metabolic rate was +34 per cent. The electrocardiogram revealed a cardiac rate of 84 beats per minute, and sinus rhythm. Left

ventricular preponderance was evident. There was an inverted T-wave in Lead I, an exaggerated T-wave in Leads II and III, an exaggerated P-wave in Leads II and III, and a notched P-wave in Lead III. Complete right bundle-branch block, with a QRS interval of 16/100 second, was found. The roentgenogram of the thorax gave evidence of a large, rounded mass in the left upper part of the thorax, with apparent atelectasis of the upper lobe of the left lung.

A diagnosis was made of a large intrathoracic tumor occupying more than half of the upper left thoracic cavity, and causing complete collapse of the upper lobe of the left lung, with marked erosion of the ribs and spinal column, for which operation was advised.

December 20, 1930, under intratracheal ethylene and gas anesthesia, the seventh rib was partially resected and the sixth rib was cut. Then complete transpleural removal of the tumor was performed. The left lung was completely collapsed, and was extremely adherent to the tumor. The third and fourth ribs were markedly eroded. These ribs were markedly eroded close to their spinal attachment. The tumor probably originated from the sheath of the spinal cord nerve just within, or immediately outside of, the intervertebral foramen, between the third and fourth ribs. The tumor produced sufficient pressure to cause marked pressure-erosion of the spinal column in this region. Although there was no tumor within the intervertebral foramen or spinal cord, there was definite communication with the large intervertebral foramen and spinal cord. From this eroded portion there was considerable hemorrhage, which was controlled by suture and by lightly packing the cavity with gauze. A small bronchial fistula was present, as a result of fixation and penetration of the tumor into the pulmonary tissue. The upper part of the left lung was completely collapsed, and only a portion of the upper part of it could be reinflated under pressure. There was marked oozing from the entire pulmonary surface from which the tumor was removed. Many of these points were ligated. The thoracic cavity was washed out with saline solution, and the chest was completely closed without drainage. The operation was extremely difficult because of the huge size of the tumor, the erosion of bone, and the adhesions of the tumor to the pulmonary tissue.

Microscopic study of the tissue revealed a neurofibroma, with fairly marked lipoid degeneration, and inflammatory portions. It weighed 675 gm. and measured 13 by 11 by 10 cm.

The man stood the operation very well, considering its magnitude. His immediate convalescence was satisfactory, with the exception of complete block of the spinal cord, due to hemorrhage into the cord, and present at the time of operation. Thirty hours after removal of the tumor, Dr. Adson performed laminectomy and found the hematoma in the cord. The operation was performed under local anesthesia, and the patient stood the procedure very well. On the following day there was some improvement in motion of the right leg, and slight improvement in that of the left leg. The man's condition remained about the same, with some slight improvement until the fifth postoperative day. On the fifth postoperative day, about 400 c.c. of bloody fluid were aspirated from the thorax, but on the sixth day only a slight amount of blood-tinged fluid was present. At that time, there was slight increase in pulse rate, with considerable dyspnea. On the morning of the sixth day, the dyspnea was very marked, and generalized convulsion developed, with spasmodic contraction of both arms. The man became comatose, and died about three hours later.

Necropsy revealed bilateral bronchopneumonia and stenosis of the isthmus of the aorta, with hypertrophy of the heart (625 gm.; normal, 275 gm.). The ductus arteriosus was patent. Arteriosclerosis of the aortic arch and coronary arteries was graded 2 and that of the descending aorta was graded 1.

This case exemplifies the increased hazard of these operative procedures when they are delayed, when there are complicating lesions due to pressure of the tumor, and when cardiac lesions are present. The tumor in this case was not of the hourglass or dumb-bell type, for there was no tumor within the spinal cord. The growth originated just outside the intervertebral foramen, and had produced sufficient pressure-erosion to enlarge the foramen and produce dilation of the blood vessels within the spinal cord. This dilation of the blood vessels was also due to the congenital anomalous condition of the heart and blood vessels. Following removal of the tumor, the hemorrhage outside the cord was readily controlled, but there had been sufficient hemorrhage within the spinal canal to produce paralysis, requiring laminectomy to relieve the pressure on the spinal cord. Cardiac function and circulation were maintained fairly well during and following both operative procedures, until the development of a pleural effusion on the side of the operation, when the patient began to show signs of cardiac failure and pulmonary congestion. This was followed by bilateral pneumonia, which was the immediate cause of death.

CASE 3.—A woman, aged twenty-five years, came to the clinic June 16, 1930, because of spells of smothering of fourteen months' duration. She had always been somewhat weak and anemic. Her general health had been as good as usual until about fourteen months before her admission to the clinic, when she had begun to have the spells of smothering that have been mentioned. At first, these attacks had occurred about five or six times a day, following exertion, and usually had been relieved by rest. Her condition had been diagnosed as heart disease, for which she had been placed under treatment, and the number of spells had become less, but the weakness had increased. Six months before her admission, roentgenologic examination had revealed the shadow of a tumor in the upper right portion of the thorax. This had been diagnosed as a malignant tumor. The woman had been given roentgen treatments, but improvement had not been noted. In the six months before her admission, she had been in bed almost constantly. The attacks had lasted only a few seconds, and had not been associated with orthopnea, dyspnea, cyanosis, hemoptysis, expectoration or cough. The spells had frightened her considerably. In the year before she came to the clinic she had had some indigestion, she had vomited some after meals, and she had been conscious of considerable pressure in the stomach. Two months before her admission she had complained of a sensation of choking after the spells of smothering, and the choking had been associated with difficulty in swallowing. This symptom had continued until the time of her admission. She had lost 20 pounds (9 kg.) in the last year. She had complained of some numbness and coldness of the left hand during spells.

Physical examination gave essentially negative results. The systolic blood pressure was 104 mm. of mercury and the diastolic 70 mm. The value for hemoglobin was 60 per cent; erythrocytes numbered 3,400,000 and leucocytes 7,300 per cubic millimeter of blood. The Wassermann reaction of the blood was negative. An anteroposterior roentgenogram contained a circumscribed shadow, in the upper portion of the thorax, extending to the first and second ribs anteriorly. The lateral roentgenogram contained a circumscribed shadow in the upper right portion, involving the entire apex, and extending to the vertebrae posteriorly. Roentgenograms of the esophagus, cardia, and stomach were negative.

Clinical résumé of her findings gave the impression that she was suffering from chronic nervous exhaustion, with many functional symptoms which were probably aggravated by the fact that she had been in bed for the last six months. It was difficult to evaluate how much the symptoms were due to the intrathoracic tumor. It was thought, however, that the tumor was a factor in the dyspnea that came on with exertion. The constant worrying over its presence was a factor in her symptoms of nervous exhaustion. She was placed under observation and treatment, and her general condition gradually improved coincident with increase in strength and some increase in weight. After a month of conservative treatment, her condition improved sufficiently so that it was thought best to remove the tumor.

July 23, 1930, under intratracheal ethylene and oxygen anesthesia, transpleural, complete removal of the tumor was performed. A posterolateral incision was made along the vertebral border of the scapula, and about 12 cm. of the fifth rib were resected. The pleural cavity was opened through the posterior periosteum of this rib. On exploration, the tumor was found to involve the entire apex of the right thoracic cavity, and the entire upper right lobe of the lung was completely collapsed over its surface. The tumor was very adherent, much more so than tumors of this type generally are; probably this was the result of the roentgen therapy. There was considerable difficulty in dissecting the lung away from the tumor, and the dissection was followed by moderate oozing of blood from the entire portion of the lung which had been adherent to the tumor. After the lung had been separated from the tumor, the tumor was enucleated with very little difficulty. It seemed to originate in the third intercostal space, probably from the third intercostal nerve. The lung was completely reinflated, and the thorax was closed without drainage.

Microscopic study disclosed that the tissue was a hemorrhage neurofibroma, with marked lipoid degeneration. The tumor measured 11 by 9 by 9 cm. and weighed 100 gm.

The woman's immediate reaction following operation was satisfactory. Her pulse rate remained approximately 110 beats per minute for the first day. On the second day, her pulse rate increased to 130, and a roentgenogram gave evidence of pleural effusion. On aspiration, about 400 c.c. of bloody fluid were removed. The patient was given a blood transfusion and was placed in an atmosphere of oxygen. On the second day, the pulse rate dropped to 120 and respirations to 24 per minute. Her condition seemed to be improved. Again aspiration of the pleural cavity was carried out, and about 200 c.c. of bloody fluid were removed. On the third day, her temperature was normal, and her pulse rate had dropped to 110 beats per minute. There was gradual improvement in her general condition. On the night of the third day, an attack of dyspnea suddenly developed and her pulse rate increased to 136 beats per minute, her respirations to 26 per minute, and she died about thirty minutes after the onset of the attack.

Necropsy revealed myocardial degeneration and about 500 c.c. of bloody fluid in the thoracic cavity. Death was attributed to cardiac failure resulting from myocardial disease, and augmented by pleural effusion.

From a clinical standpoint this case exemplifies the difficulty of evaluating the symptoms of organic disease when they are complicated by complaints of many functional disorders originating in associated nervous exhaustion. The most prominent subjective symptom in this case was produced by the cardiac disease. The many functional disorders were of long standing, but were greatly augmented following knowledge of the presence of a tumor in the mediastinum which was

thought to be malignant and was treated as malignant by application of roentgen rays. The most important symptoms produced by the tumor were difficulty in swallowing, and dyspnea due to pressure on the esophagus and trachea.

From a surgical standpoint, the cardiac disease was of paramount importance and exemplifies the increased risk of intrathoracic operations on patients who have cardiac degeneration even though there have been no severe attacks of decompensation. The operative procedure was without incident except for the increased trauma to the pleura due to the excessive adhesions which probably resulted from the previous roentgen

Fig. 5.—(Case 4.) Large tumor (neurofibroma) filling the entire lower left thoracic cavity, causing complete collapse of the lower lobe of the left lung and pushing the pericardium forward.

therapy. Cardiac function was sufficient to withstand the immediate shock of the operation, but there was not sufficient reserve force in the degenerated heart muscle to carry the patient over the most critical period of the convalescence, which is the period associated with pleural effusion.

CASE 4.—A man, aged forty-five years, came to the clinic March 8, 1934, because of arthritis of one year's duration, and also because evidence of an intrathoracic tumor had been found accidentally by roentgenologic means. About a year before his admission, both knees and ankles had become swollen, hot, and painful; there had not been any associated fever. The condition had been diagnosed as acute

arthritis, and the man had been sent to a hospital, where he had been given diathermy, without relief. In the course of the examination at the hospital a roentgenogram of the thorax had been taken, and a large shadow had been found in the lower part of the left pleural cavity. There had been no signs of pulmonary disease except a moderate cough in the morning, which was probably due to excessive smoking. The man came to the clinic primarily for treatment of the arthritis, and for advice as to the thoracic condition. He was given roentgen therapy for

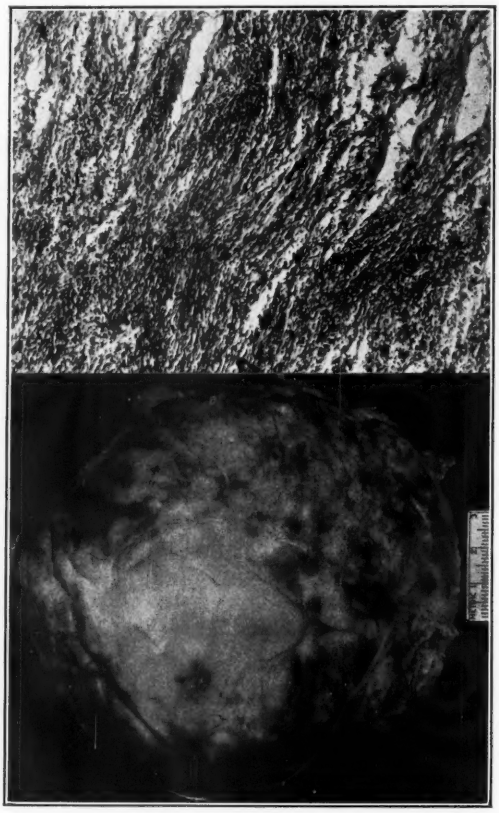

Fig. 6.—(Case 4.) Tumor and photomicrograph. Neurofibroma measuring 14 by 13 by 8 cm., and weighing 825 gm.

the arthritis, and was advised to have operation for the intrathoracic tumor after his condition had improved.

He returned to the clinic April 11, at which time examination of the thorax revealed slight dullness and diminished breath sounds at the left base, and many whistling râles in both apices, especially on inspiration. There was a diffuse apex beat and the heart was slightly enlarged. Both ankles were swollen to grade 2, and were stiff, and both knees were swollen to grade 1. There was clubbing of fingers and toes. The man's weight was 165 pounds (74.8 kg.). The systolic blood pressure was 128 mm. of mercury, and the diastolic 88 mm. The pulse rate was 84

beats per minute. Urinalysis gave negative results, except that an occasional pus cell was present. The value for hemoglobin was 88 per cent. A flocculation test for syphilis was negative.

Roentgenograms revealed a large, circumscribed shadow in the region of the posterior, lower part of the left lung (Fig. 5). Lateral views disclosed a large tumor in the lower right and posterior part of the thorax, with no involvement of bone. The tumor was thought to be benign.

A diagnosis was made of left posterior mediastinal neurofibroma, extending from the sixth to the eleventh ribs.

April 14, 1934, complete extrapleural removal of the tumor was performed under intratracheal anesthesia with ethylene and ether.

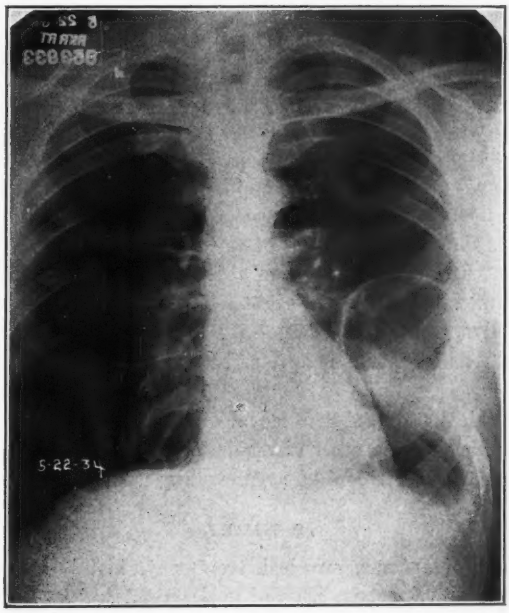

Fig. 7.—(Case 4.) Five weeks after extrapleural complete removal of the tumor. Lung almost completely expanded. Small amount of fluid in cavity which remained after removal of the tumor from the posterior mediastinum.

A posterolateral incision was made between the seventh and eighth ribs. The posterior half of the eighth rib was resected first, and immediately a tumor was encountered in the posterior mediastinum. The posterior half of the seventh rib was then removed, and it was possible completely to remove the large tumor. The tumor seemed to originate between the seventh and eighth ribs, in the posterior mediastinum, and filled the entire lower left thoracic cavity, causing complete collapse of the lower lobe of the left lung and partial collapse of the upper lobe. It extended across the entire thoracic cavity, and caused considerable pressure on the heart and pericardium, to which it also was attached. There were multiple bleeding points throughout the posterior mediastinum, on the visceral and parietal pleura, to which the tumor had been firmly attached. These bleeding points were all ligated with catgut. This was done without opening into the pleura at any

point. The lung was inflated as much as possible, and the air was aspirated from the posterior mediastinal pocket, by suction, during closure of the wound. The wound was closed by suturing the posterior periosteum of the eighth rib, obliterating the pocket posteriorly as much as possible. The thoracic wound was completely closed without drainage.

Microscopic study of the tissue revealed a neurofibroma measuring 14 by 13 by 8 cm., and weighing 825 gm. (Fig. 6).

The patient was placed in an oxygen tent immediately after operation. This was particularly indicated in his case, because of chronic bronchitis. Convalescence was uncomplicated; administration of oxygen was gradually decreased and was entirely discontinued on the fourth postoperative day. Pleural effusion did not develop, but an effusion appeared in the retropleural space, from which the tumor had been removed. This effusion gradually was absorbed and did not require aspiration. The man was dismissed from the hospital two weeks after operation, and from our care three weeks after operation, at which time the wound was entirely healed, and the roentgenogram of the chest was practically normal, except that a slight amount of fluid remained in the encapsulated retropleural pocket (Fig. 7).

This patient did not present any signs or subjective symptoms, and the tumor was found accidentally in the course of examination for arthritis. The tumor was the largest which I have removed from the posterior mediastinum. The absence of clinical symptoms in this case, I believe, was due to the position of the tumor in the lower part of the mediastinum. In one other case of this series the tumor was in practically the same situation in the right side of the thorax, but the patient had marked dyspnea. The dyspnea was due to a recent bloody pleural effusion; there had been no symptoms before development of the pleural effusion.

From a surgical standpoint, removal of the tumor in this case was less complicated than in most cases of mediastinal tumor. It was one of two cases in which the tumor could be removed by an extrapleural operation.

SUMMARY

The clinical symptoms, surgical treatment, histologic findings and operative results in fourteen cases of mediastinal and intrathoracic perineurial fibroblastomas are summarized. Four cases are reported in detail. The most important consideration in the surgical treatment is early recognition of the tumor and its immediate surgical removal, regardless of the amount of symptoms caused by it. The most important indication for surgical intervention in these cases is the possibility of the tumor undergoing malignant change. Even though these tumors remain benign, grave complications may result from pressure on the surrounding structures, particularly the spinal cord, trachea, esophagus, and lungs. The technic of operative removal of these growths depends on the indications in each case. The posterior approach is utilized when possible, and in all cases in which the growth is in the posterior mediastinum. In those cases in which the tumor is in the lateral thoracic wall, the incision is made directly over the growth. The tumors should be

removed in one stage. Extrapleural operations should always be attempted, but in most instances in this series, a transpleural operation was necessary because of adhesions and the situation of the growth. The surgical risk is greatly increased by cardiac lesions. In this series of fourteen cases there were two operative deaths; each of the two patients had associated cardiac disease. The one patient in this series who had a malignant tumor died two and a half years after operation, from recurrence. The eleven patients who had benign tumors and who survived operation are living at present, without evidence of recurrence of the tumor, and completely relieved of symptoms, from one to seven and a half years after operation.

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DISCUSSION

DR. PHILLIPS.—There is one thing that I should like to call attention to in these groups of tumors. Recently, I had four similar tumors, and in two of them there were xanthoma cells present, and they dominated the picture. In looking up the record, I found that in 1919 one of those was reported (by Jacobeus), and around 1923 Dr. Heuer reported one. Mr. Edwards showed one in 1927, and these two cases that I have had recently make five of these tumors. I do not know what the significance is. The tissue in the tumor is made up of foam cells.

PLEURAL AND PULMONARY LESIONS RESULTING FROM INTRAPLEURAL INJECTION INTO RABBITS OF MYCOBACTERIUM TUBERCULOSIS*

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IN A PREVIOUS study we presented the cytologic reactions of the pleura of the rabbit to Mycobacterium tuberculosis (bovis). At that time we indicated that the first reaction was a mild one, which was accompanied by a small exudation of serum, erythrocytes, polymorphonuclear leucocytes, lymphocytes, and a few mononuclear cells, presumably derived from the circulating blood. Phagocytosis of all bacilli had occurred within six hours. Polymorphonuclear cells began to be disintegrated, and in twenty-four hours had disappeared; at seventy-two hours the mononuclear cells preponderated and had become by far the most active of the phagocytes. All fluid disappeared within three days, but returned after the ninth day, when autogenous reinfection took place and sensitivity of tissues became established. Thereafter, massive effusions appeared which contained relatively few cells. Thirty days after injection, total cell counts varied from 1,000 to 15,000 per cubic millimeter of effusion. Differential counts on effusions from the pleura on the side into which injection had been made, gave the following readings: neutrophiles 6.8 ± 0.3, lymphocytes 70.0 ± 1.6, and monocytes and histiocytes 23.2 ± 1.4. On the opposite side, in which injection had not been made, the readings were: neutrophiles 16.2 ± 2.4, lymphocytes 57.4 ± 2.4, and mononuclear cells 26.4 ± 2.0. It was our belief that the preponderance of lymphocytes in these "chronic effusions" was due to the disintegration of polymorphonuclear cells and the removal of the phagocytic mononuclear cells by the lymph vessels to those regions where lesions were developed. We believed that the mononuclear phagocytes were histiocytes, and that they took part in the development of the histologic tubercles that resulted from the infection.

In this report we wish to trace in the same series of animals, tubercles both in the pleura and in the parenchyma of the lung. The situation in which tubercles develop in the lung and pleura is determined by the distribution of lymph vessels and their associated lymph nodes. The lesions themselves are made possible by residual intracellular bacteria which cannot be eliminated; these live a parasitic life within the

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cell, grow and multiply where they lie impounded, and stimulate a hyperplasia of histiocytes, which soon group themselves together to form concentric lamellae. The group of cells become of a size that permits identification, either grossly or microscopically, as tubercles.

Into the right pleural cavities of healthy adult rabbits was injected 3 c.c. of a suspension, in physiologic solution of sodium chloride, of bacilli of bovine tuberculosis from a young culture of virulent organisms. The suspension was of a density comparable to the third tube of McFarlane's nephelometer.

After the lapse of six hours, all bacteria had become intracellular, and the polymorphonuclear cell was the most important phagocytic cell.

In animals killed after the lapse of twelve hours, there was no gross or microscopic evidence of a tubercle. Intracellular organisms were found, however, in the pleural exudate that adhered to the costal and visceral pleura, and in one instance there was an aggregation of mononuclear phagocytes that might be identified as an early tuberculous lesion in the parenchyma of the lung.

The pleural lesions in these animals consisted of exudates which had attached themselves to the pleura and were made up of erythrocytes, lymphocytes, mononuclear cells resembling clasmatocytes, many polymorphonuclear cells, and débris resulting from the disintegration of polymorphonuclear cells. The living polymorphonuclear cell was actively phagocytic and contained one or more bacilli of bovine tuberculosis within its protoplasm. The clasmatocytes were vacuolated, very actively phagocytic, and contained not only bacilli in their cytoplasm, but also many nuclear fragments as well as polymorphonuclear cells that had retained their cellular integrity and, in some instances, still had bacilli in their cytoplasm. As yet there was no aggregation of cells which could be identified histologically as a tubercle. All the cells required in the construction of the tubercle were loosely grouped in the exudate. The exudate attached to the costal pleura resembled an infiltrative process; the cells insinuated themselves between muscle fibers much as malignant cells penetrate into tissues. Phagocytic cells, both polymorphonuclear and mononuclear, could be traced directly from the pleural surface into the depths of the muscle. Here small aggregations resembled in variety of cells and in arrangement those seen in the adherent exudate. The exudate attached to the visceral pleura was also highly cellular. Polymorphonuclear cells predominated, and the same evidence of degeneration was present that was observed in the exudate adhering to the costal pleura. The attachment to the pleura was a very intimate one, the boundaries between being almost indistinguishable. Beneath the pleura there appeared a zone of tuberculous tissue, which was highly cellular and also contained large numbers of erythrocytes. Beyond this, and penetrating deeper into the parenchyma, was a second zone in which there was well-developed pneu-

monitis. The architecture of the lung was distorted by thickening of the alveolar walls with inflammatory products and filling of the alveolar spaces with serum, erythrocytes, polymorphonuclear cells, and alveolar phagocytes; these cells were often laden with bacilli. The appearance of alveolitis and pneumonitis gradually gave way to that of the normal lung as the limits of the subpleural lesion were observed.

The highly hemorrhagic character of the subpleural lesion, the large numbers of bacilli, the early necrotic changes, and the complete absence of any deliminating zone were evidences of the acuteness and florid character of the infection. Cultural methods disclosed that all the organs of the body contained Mycobacterium tuberculosis (bovis). The penetrating characteristic suggested the possibility of a wound produced by the needle during intrapleural injection. However, great precautions were used against such an accident. The entrance to the pleural sac was recognized by the use of a manometer attached to the needle, and the needle itself was especially made with a very short bevel, so that it would not easily wound the lung. Convincing evidence that the lesion was not produced by the needle was obtained when it was noted that the situation of the lesion itself did not correspond to that traversed by the needle.

Three days after injection, definite cellular groupings were found in the depths of the intercostal muscle on the side of the injection. At this time the pleural effusion was absorbed. Also three days after injection, a wedge-shaped lesion, made up of a grouping of cells containing bacilli in their cytoplasm and accompanied by large numbers of erythrocytes, was found in the subpleural parenchyma. A small mass of cellular exudate, made up of mononuclear phagocytes, erythrocytes, polymorphonuclear cells, and débris from degenerating cells, was attached to the visceral pleura immediately overlying the parenchymatous tubercle.

On the sixth day we observed the first aggregation of cells resembling a histologic tubercle. A small bit of adherent exudate had taken on spherical form, the mononuclear cells resembled young epithelioid cells and had begun to arrange themselves in concentric zones. The outermost zone consisted of small mononuclear cells, probably lymphocytes. The inner zones consisted of cells resembling epithelioid cells which were exercising their phagocytic function. A central necrotic region was not seen, giant cells were not present, and there was no evidence of transformation of the histiocytes into cells resembling fibroblasts. Envelopment of the tubercle by fibrous tissue was entirely wanting.

Fluid reappeared in increasing amounts after the ninth day. Reaccumulation of fluid was the specific response of the body to reinfection. The cytologic response varied with the intensity of the allergic reaction to reinfection.

In the experiment which lasted twelve days, lesions were found that were similar to those which appeared after three and six days, respectively. The pleural lesions were somewhat larger and were made up of tuberculous granulation tissue. Many small vessels had penetrated the adherent exudate, so that it had become highly vascularized. Necrotic foci were scattered throughout, and recognizable caseation had developed. Many bacilli were intracellular, but many others were free and lying among the fragments of nuclei of degenerated cells. Among the marginal cells of one of the necrotic foci there were easily recognizable epithelioid cells and an occasional cell showing mitosis. One cell of this type was especially conspicuous, and it was an illustration of the metaphasic stage of mitosis.

The exudates adherent to the parietal pleura were very similar to those of the visceral pleura. They also were vascularized. Tuberculous tissue had penetrated the pleura, and an advancing edge sent digitations of cells bearing bacteria deep into the intercostal muscle. The connective tissue between muscle bundles and the spaces between muscle fibers contained phagocytic mononuclear cells. At this stage of infection it was not possible to identify the lymph vessels by a grouping of tubercles along their course.

Occasional small, young, cellular tubercles were found situated in the subpleural pulmonary parenchyma. They were definitely recognizable cellular tubercles made up of epithelioid cells and surrounded by lymphocytes. The adjacent pulmonary tissue gave evidence of invasion with the development of tuberculous alveolitis. The process was acute, tubercles were not invested by fibrous connective tissue, and there was neither necrosis at the center of the roughly spherical tubercles nor formation of giant cells.

Within the first four weeks, and thereafter, massive effusions began to fill the pleural sac. They were opalescent, straw-colored, serous effusions containing a few erythrocytes, or else they were frankly serosanguineous, containing large numbers of erythrocytes. Uncontaminated purulent effusions were not encountered in these experiments. Massive purulent effusions have been encountered only in sensitized animals which had received a very large sensitizing dose of virulent bacilli. We believed that the effusions became massive because of two factors. The first factor was that the pleura was being continuously subjected to reinfection by autogenous addition of relatively small numbers of bacilli. Bacillary invasion of autogenous character acting on the sensitized pleura produced allergic reactions so that inflammatory manifestations resulted. The objective result was a large quantity of serosanguineous fluid that remained for a much longer time than the smaller amounts of fluid which succeeded the first infection of an unsensitized pleura. The second factor influencing the size of the effusion was the speed of resorption. With a normal

lymphatic system for drainage, fluid and bacteria were very promptly removed from the pleural sac. Within from forty-eight to seventy-two hours the small, first effusions had disappeared and the pleural sac had been dry. The fluid resulting from autogenous reinfection was not absorbed as readily, not only because there was much more of it, and it was richer in protein, but chiefly because it was continuously reforming and because the lymphatic system was blocked by the development of tuberculous tissues throughout its course.

Four weeks after intrapleural inoculation, typical mature tubercles

Fig. 1.—Three-day experiment. Intercostal muscle; histiocytes and phagocytosed bacteria are present.

were scattered throughout the lung. Miliary tubercles were found in the liver and spleen.

In experiments which lasted from six to eight weeks, generalized tuberculosis had begun to develop in the animals. Miliary tubercles were present in the spleen, liver, and kidneys, as well as in the pleura, both parietal and visceral, and in the lung on the side that had received the inoculum. There was a singular absence of gross and microscopic tubercles in the opposite lung and pleura, even though, as we have reported elsewhere, fluid in small amounts collected in the pleural space. On the affected side, the parietal pleura was thickened,

and studded with large and small masses of hyperplastic tubercles which were arranged segmentally corresponding to the course of lymph vessels. The diaphragmatic and the visceral pleura were similarly affected by implants of tuberculous tissue, although to a lesser degree than the parietal pleura, and with less evidence of systematic or purposeful distribution. Gross evidence of enlargement of the superior and inferior tracheobronchial, paratracheal, posterior mediastinal, and sternal lymph nodes had occurred as early as the eighteenth day; by the eighth week, however, these structures were frequently extremely en-

Fig. 2.—Twelve-day experiment. Pleural exudate made up of tuberculous granulation tissue. Areas of necrosis are present, also typical epithelioid cells containing bacilli of tuberculosis in their cytoplasm.

larged, almost to the size of tumors, and they filled the mediastinum and obscured and compressed the heart and lungs.

Wherever tuberculous tissue had attached itself to the visceral pleura, the underlying pulmonary tissue had become invaded and had been replaced by large, single or confluent tubercles. Without doubt the bacilli escaping from these foci had been caught and transported by the current of lymph and deposited in tissues rich in lymph vessels wherein the lesions had developed. Tubercles in various stages of development could be seen in perivascular and peribronchial pulmonary

parenchyma and, sometimes, they were of such a size that they completely surrounded the smaller bronchi.

In the majority of the discrete subpleural tubercles there was a central zone of caseous material, surrounded by concentrically arranged zones of epithelioid cells and an investing zone of lymphocytes. Rarely, a giant cell was seen and distinguished because of the number and arrangement of its nuclei, its protoplasmic projections, and the presence of Mycobacterium tuberculosis (bovis) within its protoplasm. In almost every instance the severity and acuteness of the infection were

Fig. 3.—Thirty-day experiment. Subpleural tubercle with necrotic area eroding the pleura; bacilli are free to enter the pleural space.

shown by the entire absence of fibrous connective tissue and by the encircling zone of tuberculous pneumonitis, which obscured the boundaries of the tubercle. In certain tubercles it was observed that the caseous region was eccentric in situation and was ineffectively bounded by the visceral pleura. In such cases acid-fast bacillary forms, both intracellular and free, were present in large numbers, and they had free access to the pleural sac.

The peribronchial tubercles were of similar construction to the subpleural tubercles. In two animals that survived thirty and thirty-four days, respectively, ulcerative phenomena determined the spread of

this infection. In the former, a tubercle completely surrounded a small bronchiole and had invaded the wall. The lumen was filled with exudate in which intracellular bacilli were demonstrable. In the latter, the animal died of pneumonia due to ulceration and destruction of its bronchial wall and emptying of the necrotic material from the tubercle into the lumen. Many bacilli were poured into the lumen of the bronchus, and bronchonpeumonia developed. In this same animal a perivascular tubercle had ulcerated into the wall of a vein, and the intima alone separated the tubercle from the circulating blood.

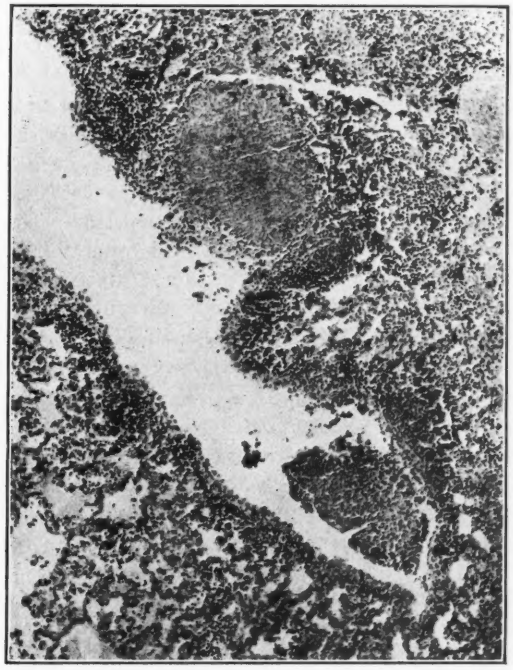

Fig. 4.—Caseous tubercle in the peribronchial tissue with erosion through the bronchial wall and broncial exudate containing bacilli.

In experiments lasting eight weeks and longer, large tuberculous masses outlined the course of the lymph vessels, enlarged the regional lymph nodes, and created tumorlike thickenings in the mediastinum.

In animals that survived twelve weeks, the lungs were grossly tuberculous; and, on microscopic examination, diffuse tuberculous pneumonitis was demonstrable in which discrete tubercles or caseous foci were interspersed. The segmental lymph vessels and all thoracic lymph nodes were involved, and the abdominal organs contained miliary tubercles. Occasionally, the wall of the thoracic duct was thick-

ened and nodular, and masses of tuberculous tissue 0.05 cm. in diameter, occupied the wall of the cisterna. All the lymph nodes in the vicinity of the cisterna were filled with tuberculous material, and those related to the kidney were enlarged, firm, and definitely tuberculous. The mesenteric lymph nodes were not involved in any of the animals used in these experiments (Figs. 1-4).

CONCLUSIONS

When virulent organisms of Mycobacterium tuberculosis (bovis) are introduced into the pleural space of healthy rabbits, they constitute foreign bodies of the particulate type to which tissues react with a nonspecific form of inflammation. The fluid and cellular parts of the resultant effusion are promptly resorbed, carrying with them the particulate material, which had been phagocytosed, and depositing it in regional lymph nodes and in remote organs. Many of the intracellular bacilli could not be removed, but remained within the lymph spaces or were included in cellular masses attached to the pleural surfaces. Up to this point, the reaction is entirely nonspecific. Thereafter, the reaction becomes specific because the particulate matter is made up of living organisms and is capable of growth and division. Non-sensitive tissues are changed to sensitive tissues, and allergic reactions respond to reinfection as vast numbers of virulent bacilli are released into the tissues. The massive, persisting effusions are objective evidence of a specific response to reinfection.

Tubercles develop on pleural surfaces as a result of persisting irritation of residual bacilli, and represent hyperplasia of histiocytes and regional fibroblasts. Epithelioid cells and giant cells appear as developmental changes in histiocytes. Similar tubercles develop in the parenchyma of the lung, in the regional nodes, and in remote organs wherever residual bacilli are harbored, and are increased in numbers by growth of organisms. Caseation and ulceration of tubercles into the lumen of bronchi and veins constitute hazards to the life of the animal by providing a means of rapid transport of organisms to uninfected tissues. The acute reactions and the lesions which bring about illness and death are final evidences of a specific reaction.

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THE CHEMICAL DESTRUCTION OF PERIOSTEUM IN THE TREATMENT OF CHRONIC EMPYEMA*

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THE radical treatment of the tuberculous postpneumothoracic fistulous empyema is one of the most difficult surgical problems both because of the intrinsic difficulties and because of the bad general condition of the patients who are in need of this treatment. And yet the question has a great social importance because of the large number of subjects relatively young and able to recover who are suffering from this consequence of pneumothorax treatment.

The description of some cases I have observed and operated on among the various patients of our Hospital Sanatorium S. Luigi of Turin may demonstrate, better than a theoretical discussion, the reality and the importance of such difficulties.

The greatest difficulty in obtaining a recovery from empyema is in the abolition of the suppurating cavity; so that the most promising intervention is the resection of the thoracic wall following the directions given by Schede. It is, however, useful to note that the Schede method was described prior to pneumothorax treatment and was considered only for the treatment of empyemas which had begun in healthy subjects, becoming chronic and fistulous only at a later time. The Schede method is then suitable, without substantial risks, in the treatment of usual empyemas, but it is not possible to use it for tuberculous patients without modifying it accordingly. Tuberculous patients must be operated on under local anesthesia, and consequently resections must be very limited in such a way that the operation may be divided into various stages.

The patient shown in Fig. 1 was a young man, twenty-eight years of age, who was admitted to our hospital after having been operated on twice in another clinic of our city, one year and a half after the first pleurotomy. He went out cured and returned to work after having undergone, in two years of treatment, eight partial resections of the thoracic wall following the Schede method, all under local anesthesia.

Not all patients have sufficient resistance to tolerate, without dangerous complications, such repeated interventions. Sometimes after very limited interventions septic complications arise with fever lasting for from thirty to forty days, so that it may happen that it is necessary to wait three or four months from one intervention to the next; and if

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the patient is in poor condition, it is very difficult to complete the whole operation.

Fig. 2 shows the thoracic lesion of a patient after the second stage: flaps of the thoracic wall obtained after a partial pleuro-osseous resection had no tendency to adhere to the pleuropulmonary wall and remained in continual movement. Septic fever arose and the patient died of chronic sepsis and marasmus before the end of the operative treatment.

Practically the same condition is presented by the patient shown in

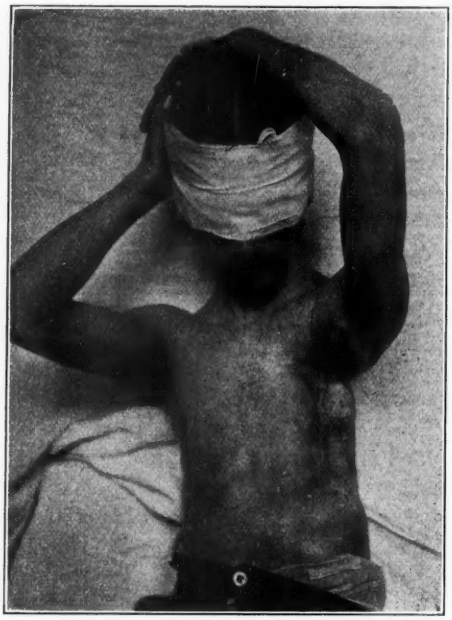

Fig. 1.

Fig. 3 with the difference that she tolerated sufficiently well three interventions. She is still living and without fever, but she is in such a condition of marasmus and amyloidosis that although the last operation was made more than two years ago, her condition does not warrant attempts to perform the final stages of the operation.

These three cases were selected from a series of ten patients upon whom I operated by this method, obtaining three decisive recoveries; three patients died, and in the other four cases the treatment could not be completed because of the bad condition of the patients.

On the basis of these experiences, I can conclude that the Schede method, which theoretically should represent the best and ideal method

for the treatment of chronic fistulous empyemas, practically is too complicated and severe, so that it cannot be used for all patients. Also in the fortunate cases in which recovery is obtained, the result is secured only at the cost of numerous interventions with very long periods of discomfort and residence in special hospitals.

The thoracic resection of Schede is, on the contrary, really adapted for the treatment of empyemas occupying only a part of the hemithorax. Four patients with such conditions were operated on by me

Fig. 2.

in two or three stages, and they all recovered with the total obliteration of the suppurating cavity. But the inconstancy and severity of the Schede method render it advisable to give the preference to the Estlander procedure, which allows the operator to stay away from the infected pleura and is, in itself, a less severe operation and surgically more nearly correct because it involves only zones which are not infected. But the Estlander method, when used for tuberculous patients, does not always give the desired result. The following are some examples:

Fig. 4 illustrates a case of a total fistulous empyema recovered in a few months after a total extrapleural thoracoplasty performed in two stages. The empyema was of three years' duration, and the fever was moderate; the patient left the clinic perfectly recovered and was able to return to his occupation of teaching. On the contrary, in the case shown in Fig. 5 the same intervention was not sufficient to produce complete recovery, and suppuration from the anterior fistula still persists. Also in the case shown in Fig. 6, notwithstanding the very wide resection of ribs, the patient did not recover.

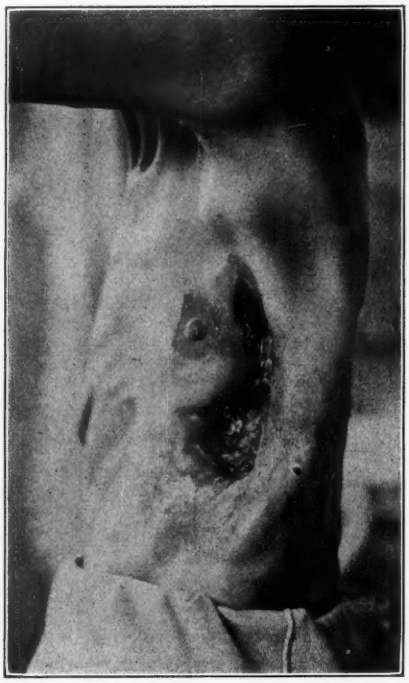

Fig. 3.

The explanation of these failures is obvious. If the periosteum is saved, it is possible for the formation of new ribs to render the thoracic wall rigid again before the empyema cavity is completely obliterated. Our patients are not robust with rapid reactions: they are wasted people, and in them the reduction of the thoracic cavity is only a mechanical means of offering the possibility of recovery. In such patients, after the cavity has been reduced, the specific pleuritic process must be allowed to recover, a procedure which is necessarily slow and chronic. Consequently before the end of the healing process the formation of new ribs occurs which produces a rigidity of the thoracic

Fig. 4.

Fig. 5.

wall: the cavity will be reduced to smaller dimensions, but it will also be a rigid cavity and consequently incurable. A typical example is

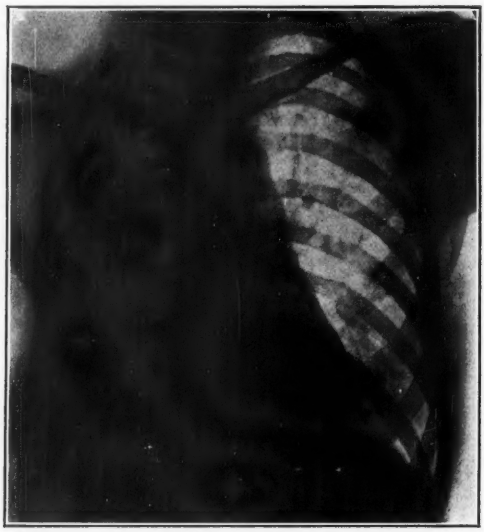

Fig. 6.

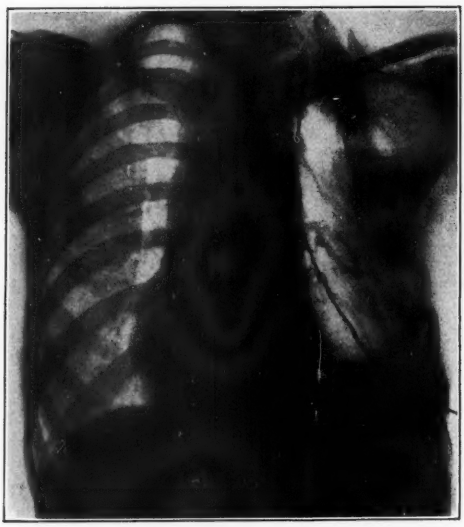

Fig. 7.

the patient in Fig. 7, in whom, notwithstanding the anterior drainage and the wide removal of bone, there exists a large cavity which is

kept open by the strips of newly formed bone which are plainly visible in the roentgenogram.

The recent studies published by C. M. Van Allen[1] on the chemical destruction of periosteum for the purpose of preventing new rib formation, are destined to be of great advantage to surgeons who are interested in these questions. With a full appreciation of the importance of the help from such a technical expedient, I desired to try it.

Figs. 8 and 9 refer to a case of fistulous chronic empyema from pneumonia lasting for one year with night fever reaching 38° and 39° C. in spite of sufficient drainage. The volume of the thorax and the strong musculature rendered anatomically grave an extensive removal by the Schede method. On the other hand, an extrapleural thoracoplasty to be made in several stages without the resection of the periosteum could not be sufficient to obliterate the enormous cavity. I

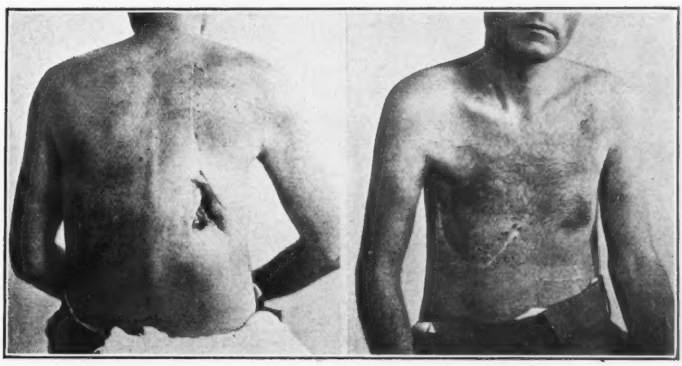

Fig. 8. Fig. 9.

thought of combining the two methods, Schede and Estlander, resecting the periosteum without removing the parietal pleura, but technically it was not possible to be certain of doing so without injuring the pleura and with the risk of provoking septic complications and still worse conditions. I therefore operated in the following manner: I raised an extensive cutaneous muscle flap and resected the maximum length of ribs from the sternum to the axilla, painting generously the periosteal beds with Zenker's solution. Then I replaced the flap and sutured the wound completely; this healed rapidly without suppuration. After twenty days, I performed a posterior costal resection with the paravertebral incision of Sauerbruch, keeping above the fistula and removing the remaining portions of the ribs from the vertebral column on.

Two months after the operation the fever had disappeared, and suppuration was greatly diminished. The patient has not yet recovered,

but he will certainly recover because no obstacle will be presented by a new rigidity of the costal walls of the abscess cavity which can prevent the cicatrization. In fact, the roentgenograms demonstrate the absence of any bone regeneration and therefore the almost complete lack of ribs. There remain only the first rib and an isolated fragment of the fourth or fifth rib which escaped resection; the empyema is therefore entirely transformed into a usual cold abscess of the soft parts and is in the best condition for healing. (Fig. 10.)

Fig. 10.

Using the same method I operated on another patient limiting at first my intervention to the anterior flap, because there had already been an extensive posterior resection performed previously by the Schede method. Two months after the operation the patient presents an appreciable diminution of suppuration, and there is no tendency to formation of new ribs, as can be seen from the roentgenogram. (Figs. 11, 12, 13.) The wound, notwithstanding the generous application of Zenker's solution, has healed *per primam* without any necrosis or suppuration.

Fig. 11. Fig. 12.

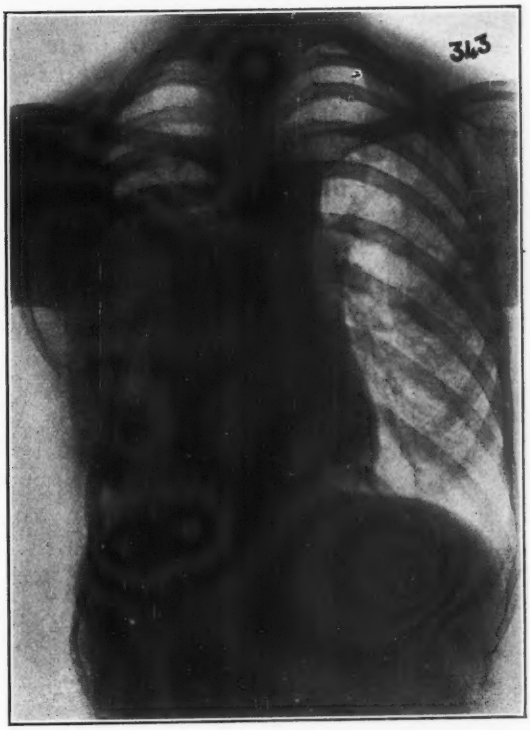

Fig. 13.

I have not experimented either on animals or on men with any other substance than Zenker's solution. This solution was already suggested by Jerome R. Head,[2] who after accurate experimental studies declared it the most suitable and least toxic solution. I have now had a certain amount of experience with this because I have used it also in some thoracoplasties for pulmonary tuberculosis (concerning the result of which I cannot yet speak conclusively). I can, however, note that Zenker's solution can be used without any hesitation when it is necessary to paint the periosteum of the anterior ribs, in which the dissection of the periosteal bed succeeds anatomically easily and perfectly, while in the back and paravertebral region the dissection of periosteum is accomplished less satisfactorily. The periosteum tears easily in irregular strips, and the Zenker's solution may be imbibed by the muscle tissue, with the consequent danger of necrosis or of not destroying the periosteum entirely.

The technic of resection for empyema is more easily compared with the technic of thoracoplasty for collapse therapy in pulmonary tuberculosis, because the ribs which cover the empyema cavity are subject to chronic inflammation, with the consequent thickening of the periosteum. This has already been noted by Bisgard,[3] and then it is easier to have in the dissection a good periosteum with a well-defined bed, to paint with the fixative liquid. I have had no experience at all with the destruction of periosteum with the electrobistoury or with the thermocautery as used by Eloesser of San Francisco.[4]

CONCLUSION

My experience refers to fifty cases of severe fistulous postpneumothoracic empyema, and from this experience I advise against a resection according to the Schede method because it is too severe. It is better to operate according to the plan of Estlander, but there is the danger of not succeeding in the complete healing of the patient because the formation of new bone again gives a rigidity to the thoracic wall and prevents the total obliteration of the cavity. The use of Zenker's solution prevents the new formation of bone, and being inoffensive it does not disturb the regular cicatrization of the operative wound and facilitates appreciably the radical therapy of chronic empyemas.

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THE TREATMENT OF PULMONARY TUBERCULOSIS BY BRONCHIAL OCCLUSION

An Experimental Study*

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Chicago, Ill.

THE fundamental principle underlying the usual treatment of tuberculosis is rest of the part. In pulmonary tuberculosis bed rest is the routine, to minimize the "exercise" action of the lungs. However, in an increasing number of cases, additional localized rest is being obtained by some form of "collapse therapy." Accompanying most forms of such therapy there is usually produced a varying amount of collapse of lung tissue.

The frequent association of spontaneous atelectasis with pulmonary tuberculosis has been repeatedly observed (Koral,[1] Loeschke,[2] Delafield and Prudden,[3] Glenn,[4] Singer[5]).

It has been commonly believed that atelectasis (spontaneous) was an unfavorable complication of pulmonary tuberculosis.[6-10] In some such cases there were no signs of increased toxicity, but symptoms resulting from displacement of the mediastinal structures, and good results have been reported following the correction of the displacement by artificial pneumothorax.

Hennell,[11] Koral,[1] Packard,[12] Jacobaeus,[13] Gotterdam,[14] and others are of the opinion that most of the so-called fibrotic lungs originate from the association of atelectasis with pulmonary tuberculosis. They have noted that the "tuberculous process may become minimal and its clinical significance relatively unimportant" in cases of chronic fibroid phthisis.

A means of investigating this problem presented itself in the development of a safe and reliable method for producing massive atelectasis in animals.[15] This consisted of cauterizing the bronchial mucosa with a 35 per cent solution of silver nitrate applied through a bronchoscope. About two weeks subsequent to the cauterization, complete stenosis of the bronchial lumen had occurred and was routinely accompanied by massive atelectasis of the obstructed pulmonary tissue.

Roentgenograms revealed the diaphragm elevated and the mediastinal structures deviated toward the affected side. At autopsy, the atelectatic

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lungs were found to be dark in color and shrunken to from one-fourth to one-sixth of their original size. A microscopic section taken longitudinally through the region of stenosis revealed complete destruction of mucosa and partial destruction of the cartilages with marked reduction in the circumference of the bronchus. The occlusion of its lumen was brought about by collapse of the rigid bronchial wall with the formation of granulation tissue, dispersed in which were the partially destroyed cartilages. A microscopic section taken distal to the region of stenosis, across an entire lobe, disclosed the larger bronchi dilated and filled with mucus; while the surrounding bronchioles and alveoli were collapsed and airless. The alveolar walls were so closely packed together that their outlines were quite indistinct. Another interesting finding was the changes that had occurred in the vascularity of the collapsed lung.[16] During the early weeks of collapse the capillaries appeared to be dilated and tortuous. After a few months had expired, sections of atelectatic tissue revealed many dilated air spaces filled with blood, hemangiomatous in appearance. By comparing microscopic sections taken before and after injection of the animal with a solution of India ink according to the technic of Coryllos and Birnbaum,[17] the vascular changes were found to consist of a marked passive congestion. Some of the collapsed tissue was reinflated in situ with its vascular supply intact. Microscopic sections taken before and after reinflation with and without injection of India ink were compared. The dilated spaces filled with blood were found to be alveoli through which blood was slowly flowing. A report of these experiments may be found elsewhere.[18]

Thus by this method of producing collapse, we obtain a passive congestion of the obstructed lung and complete rest of the part, more complete perhaps than by any other known method.

With this information at hand, and in view of the above mentioned facts concerning atelectasis and pulmonary tuberculosis, we undertook the treatment of pulmonary tuberculosis, produced experimentally, by this form of collapse.

EXPERIMENTS

At the onset we were confronted with two problems. First, how to produce the desired lesions in the experimental animals. Second, to determine what effect atelectasis would have on these lesions.

Since the relative susceptibility of the dog to human type tubercle bacilli had been previously demonstrated,[19] and since bronchial stenosis and subsequent pulmonary atelectasis were easily accomplished in the dog, as already described,[15] this species was used as the major experimental animal. A few monkeys and goats were also used. The first tuberculous lesions were of a hematogenous nature. A description of these experiments follows.

Hematogenous.—Twenty-five dogs were divided into two groups. In the first group of seventeen dogs human tubercle bacilli 0.10 mg./kg. body weight (H 119)* was injected in saline suspension into the femoral vein. In three dogs, massive atelectasis of two lung lobes was produced previous to the injection. In the remaining fourteen it was obtained from two to six weeks subsequent to the injection. One cauterization was sufficient to produce complete stenosis of the bronchi in 90 per cent of the cases. The course of the experiments was followed by fluoroscopic and x-ray examinations. Most of the animals appeared quite ill following the infection and gradually became worse. General lassitude and some loss of appetite were commonly observed. Loss in weight was present in all cases and many times this was extreme. Animals not dying of the disease were sacrificed by electrocution.[20]

Results.—A résumé of the results of this group may be found in Table I. Of the seventeen dogs, nine died of miliary tuberculosis of the lungs from ten days to thirteen weeks following infection. The remainder were sacrificed at irregular intervals, some as long as eight months after infection. A marked contrast between the atelectatic and normally inflated lobes was seen with very few exceptions throughout the entire group. Whereas the inflated lobes were studded with tubercles, the size of which varied according to the duration of the disease, the collapsed

TABLE I

BILATERAL HEMATOGENOUS GROUP

DOG NO.	TIME SINCE INOCULATION	DURATION OF COLLAPSE	RESULTS	
			INFLATED (CONTROL)	COLLAPSED
69 E	2 weeks	2 weeks	No gross tuberculosis. Microscopic tubercles and tubercle B. present.	No gross tuberculosis. No microscopic tubercles or tubercle B.
393 E	4 weeks	4 weeks	Miliary tuberculosis 1-2 mm.; 10-20 tubercle B. per H.P. field.	No definite tubercles. 10 tubercle B. in an entire section.
155 E	8 weeks	8 weeks	Miliary tuberculosis 2-3 mm.; 10-12 tubercle B. per H.P. field.	1 tubercle in 2 lobes. 1-4 tubercle B. per H.P. field.
465 E	10 days	None	No gross tuberculosis. Microscopic tubercles and tubercle B.	
470 E	17 days	3 days	Miliary tuberculosis 0.5-1 mm. Pneumonia.	No gross tuberculosis. Microscopic tubercles. Few tubercle B.
488 E	24 days	11 days	Miliary tuberculosis 1-2 mm. Few tubercle B. seen.	3 gross tubercles in 2 lobes. Very occasional tubercle B.
A	28 days	12 days	Miliary tuberculosis 1-2 mm. Many tubercles and tubercle B.	No gross tuberculosis. No microscopic tubercles. Occasional tubercle B.
472 E	38 days	25 days	Miliary tuberculosis 1-2 mm. also confluent. Many tubercle B. Bronchopneumonia	3 gross tubercles in 2 lobes. Occasional tubercle B.

*A human type strain of moderately high virulence for guinea pigs.

TABLE I—CONT'D

DOG NO.	TIME SINCE INOCULATION	DURATION OF COLLAPSE	RESULTS	
			INFLATED (CONTROL)	COLLAPSED
463 C	41 days	26 days	Miliary tuberculosis 1-2 mm.; 30-40 tubercle B. per H.P. field.	Few minute tuberculosis. Many epithelioid cells. Only occasional tubercle B.
473 E	45 days	None	Miliary tuberculosis 1-2 mm.; plus bronchopneumonia. Many tubercle B.	
153 E	52 days	37 days	Miliary tuberculosis 0.5-3 mm. Microscopic tubercles. Many tubercle B.	No gross tuberculosis.
485 E	71 days	57 days	Miliary tuberculosis 2-4 mm. Many tubercle B. per H.P. field.	Occasional tubercle ⅓ mm. Edematous. Many tubercle B.
467 E	92 days	78 days	Miliary tuberculosis 1-4 mm. confluent. Many tubercle B.	Inflated by anastomosis with right lower lobe. 5 tubercles. Few tubercle B.
484 E	127 days	113 days	No definite tubercles. No tubercle B.	Lymphocytic and mononuclear infiltration. No gross tubercle. Very few tubercle B.
478 E	161 days	147 days	Few tubercles 1 mm. Very few tubercle B.	Much edema and cellular infiltration. Occasional tubercle B.
486 E	175 days	161 days	No gross tuberculosis. Few tubercle B.	Inflated by physiologic anastomosis. No gross tuberculosis. Very few tubercle B.
479 E	225 days	211 days	Scattered tubercles 2-4 mm.; caseating tubercles and many tubercle B.	Physiologic anastomosis. No gross tuberculosis. Few microscopic tubercles and tubercle B.

lobes revealed very few or no gross tubercles (Figs. 1 and 2). Gross miliary tuberculosis did not appear for two weeks following infection. Subsequently, tubercles frequently became as large as 0.5 cm. in diameter and not infrequently became confluent. Such tubercles as were found in the atelectatic lobes were very minute, rarely reaching over 0.5 mm. in diameter. Complete occlusion of the primary bronchus of a pulmonary lobe unaccompanied by massive atelectasis of the obstructed tissue was found in three instances. This was due to a physiologic anastomosis with an adjacent lung lobe. In these cases more tuberculosis was found than in atelectatic lobes; but far less than in nonobstructed, normally inflated pulmonary tissue.

In three dogs, 69 E, 393 E and 155 E, of this series, massive atelectasis of two lung lobes was produced prior to injection of the bacillary suspension. The inflated lobes were studded with distinct tubercles, their size being directly proportional to

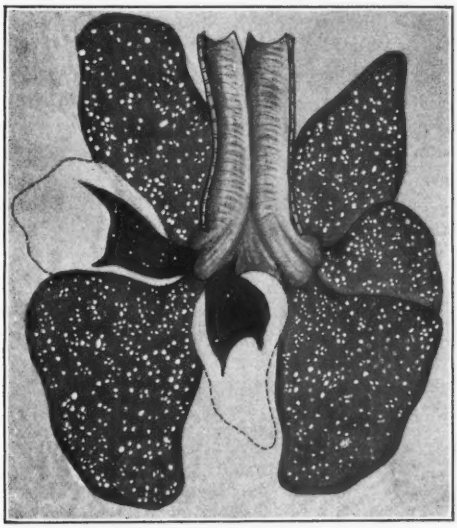

Fig. 1.—(463 C) Diagrammatic illustration of lungs of dog of the bilateral hematogenous group. Duration of infection, forty-one days. Duration of collapse of the right middle and accessory lobes, twenty-six days. The inflated lobes are studded with tubercles, whereas very few small tubercles were found on the collapsed lobes.

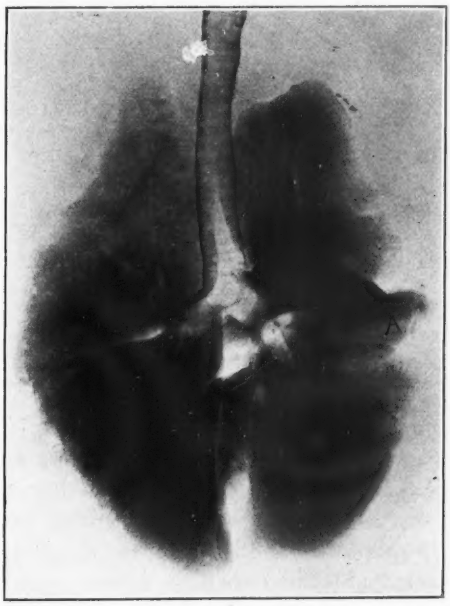

Fig. 2.—(153 E) X-ray of lungs of dog of bilateral hematogenous group. Infected fifty-two days. Collapse of right middle lobe, *A*, for thirty-seven days. X-ray evidence of tuberculous involvement of only the inflated lobes.

the age of infection. Microscopically, the tubercles were formed about blood vessels or bronchioles (Fig. 3-*A*). As the disease progressed, the tubercles by their growth had compressed and often occluded the lumina of these passages. The early tubercles were composed mainly of large nononuclear cells, lymphocytes, and few polymorphonuclear leucocytes. Epithelioid cells were just beginning to make their appearance. In late stages of infection where the tubercles were large and often confluent (Fig. 3-*B*), epithelioid cells predominated. Lymphocytes and polymorphonuclear leucocytes were less abundant, being in the majority of cases sparsely scattered throughout the tubercle. Caseation was well advanced in many of these older tubercles. Bacilli were numerous throughout all sections of the various animals. As many as twenty were often found in a single epithelioid cell of dog 155 E. The tuberculous process in all cases of collapsed lobes was not so pronounced as that in the corresponding inflated control lobes (Fig. 3-*C*). In dogs 69 E and 393 E definite tubercle formation was not observed, but there were occasional small foci of mononuclear cell increase usually perivascular in location. In dog 155 E, one small gross tubercle was observed. It was formed by a compact collection of large mononuclear cells. Tubercle bacilli were found in dogs 393 E and 155 E, but with great difficulty. Minute examination of numerous sections of dog 69 E revealed none.

In the remainder of the dogs of group 1, a massive atelectasis of two lung lobes was obtained from two to six weeks after infection. The inflated lobes in the majority of cases were air-containing, and tubercles were observed in all such tissue of the various animals. They ranged in size from 0.5 mm. to 4 mm. in diameter. Either they were composed of large mononuclear cells with lymphocytic and polymorphonuclear leucocytic infiltrations, or as in those of longer duration they were made up mainly of epithelioid cells with or without central caseation. In one dog, 463 C, an occasional tubercle was observed with polymorphonuclear leucocytes concentrated in their centers. A small ulcerative lesion had formed in dog 467 E. In other dogs, 484 E, 478 E and 486 E, where infection was of longest duration, numerous compact microscopic tubercles were found. The structure of their cellular units was indistinct because of the black and brown pigment concentrated within them. Bacilli were difficult to find in tubercles such as these. In other cases, however, bacilli were numerous. In many of the collapsed lobes, the tissue was evenly infiltrated with large mononuclear and epithelioid cells without definite tubercle formation. In other lobes small microscopic tubercles were present. They were few in number, never more than five being observed in a single lobe. Microscopically these tubercles were compact and made up of large mononuclear and epithelioid cells. Polymorphonuclear leucocytic and small round cell infiltrations were generally absent. In animals 479 E and 484 E, where infection was of longest duration, the compact tubercles contained much black and brown pigment and were infiltrated with varying amounts of fibrous tissue (Mallory stain). Throughout all collapsed lobes, tubercle bacilli were difficult to find. One would occasionally be observed in a large mononuclear cell about which there was no reaction.

In dogs 467 E, 486 E and 479 E complete collapse was not obtained because of a physiologic anastomosis between the lobe whose bronchus was completely occluded, and an adjacent respiring lobe. The tuberculous process in this occluded lobe, however, was less advanced than that in the unobstructed inflated lobes.

In general, the intensity of the disease in the inflated lung increased with its duration, whereas the reverse was true in the atelectatic lung.

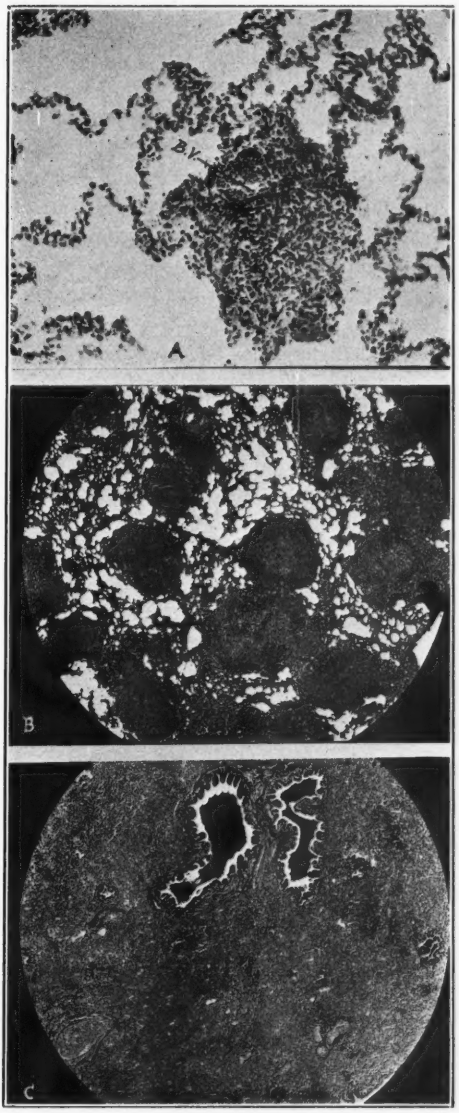

Fig. 3-*A*, (69 E) Photomicrograph of lung infected with human tubercle bacilli of two weeks' duration, showing large but lacy tubercle formation about a blood vessel.

B, (155 E) Photograph of lung infected with human tubercle bacilli for eight weeks. Note large, confluent tubercles and compare with *C*.

C, (155 E) Photomicrograph of collapsed lung of dog infected with tubercle bacilli. Both infection and collapse are of eight weeks' duration. Only one tubercle was found in the entire lobe.

These changes in both the inflated and the collapsed lobes were occurring simultaneously in the same animal.

In two instances much edema occurred in the atelectatic lobes, and here the beneficial results were not so striking. In one of these, no tuberculosis was found in the inflated lobes. This was the only exception in the entire group.

In the second group of eight dogs, a saline suspension of human tubercle bacilli (0.2 mg. H 119) was introduced into the left lung by injection into the left pulmonary artery through a thoracotomy opening. A very coarse suspension of the culture was used, in the hope that most of the organisms would remain lodged in the left lung. Massive atelectasis of the left lung was produced from two to six weeks later by complete occlusion of the left primary bronchus. In 70 per cent of this

TABLE II

UNILATERAL HEMATOGENOUS GROUP

DOG NO.	TIME SINCE INOCULATION	DURATION OF COLLAPSE	RESULTS	
			RIGHT LUNG	(INFECTED) LEFT LUNG
840 D	35 days	None	No gross tubercles. No microscopic tubercles or tubercle B.	Miliary tuberculosis. Tubercles with caseating centers. Many tubercle B.
683 E	50 days	35 days	Pneumonia (cause of death). Many tubercle B.	*Upper Lobe*— Atelectatic. No gross tuberculosis. Occasional tubercle B. *Lower Lobe*— No collapse. Miliary tuberculosis. Many tubercle B.
682 E	68 days	39 days	Miliary tuberculosis 1-6 mm. Ulcerative tuberculosis. Many tubercle B.	Atelectatic. No gross tuberculosis. 3 tubercles in entire section. 1 tubercle B. in section.
685 E	96 days	67 days	Miliary tuberculosis 1-3 mm. Confluent, ulcerative tuberculosis. Many tubercle B.	Atelectatic. No gross tuberculosis. No microscopic tubercles. No tubercle B. seen.
246 E	117 days	57 days	Scattered tubercles 1-3 mm.; tubercle B. present.	Atelectatic. No gross tuberculosis. Few small tubercles. No tubercle B.
688 E	129 days	58 days	No gross tuberculosis. Few small tubercles. Tubercle B. present.	Atelectatic. No gross tuberculosis. 1 small tubercle. No tubercle B.
247 E	181 days	121 days	No gross tuberculosis. Medium-sized tubercles. Tubercle B. present.	Atelectatic. No gross tuberculosis. No microscopic tuberculosis or tubercle B.
126 F	207 days	130 days	No gross tuberculosis. No tubercle B.	Atelectatic. No gross tuberculosis. No microscopic tuberculosis or tubercle B.

group the bronchus was completely occluded by one application of silver nitrate. The postoperative course was observed by fluoroscopic and roentgenologic examinations. These dogs appeared quite ill for a short time following infection, but with the exception of three animals, they soon became active, and after from six to eight weeks were apparently quite normal again.

Results.—A résumé of the results of this group may be seen in Table II. One dog died five weeks after infection, before any collapse was produced. Miliary tubercles with caseating centers were present in the infected left lung with many tubercle bacilli demonstrable (Fig. 4). No tuberculosis was found in the right lung. A second animal died of pneumonia of the right lung, fifty days after infection and thirty-five days after collapse of the left upper lobe. This lobe revealed no gross

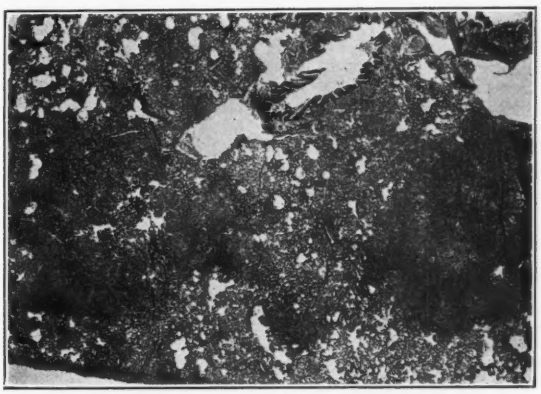

Fig. 4.—(840 E) Photomicrograph of lung of dog in unilateral hematogenous group. Duration of infection, thirty-five days. Note large tubercle with caseating center and several small coalescent tubercles.

tuberculosis, and stained sections presented only an occasional tubercle bacillus. The inflated left lower lobe was studded with tubercles, and sections revealed caseating lesions with large numbers of tubercle bacilli. X-ray examination of a third animal, eight weeks following infection and four weeks following collapse, presented evidence of tuberculosis in the right lung (Fig. 5-*A*). The left lung was collapsed. The dog died two weeks later of massive tuberculosis of the right lung, which was studded with tubercles from 1 to 6 mm. in diameter and which in many places were confluent. The injected left lung was atelectatic and showed no gross evidence of tuberculosis (Fig. 5-*B* and *C*). Only three minute tubercles were found in an entire section on microscopic examination and only one bacillus (Fig. 6-*A* and *B*). The remaining five animals were sacrificed at irregular intervals, the longest duration being two hundred and seven days following infection. The inflated right lung

in all animals, except dog 126 F, revealed gross or microscopic tubercles. In dogs 683 E, 246 E and 685 E gross tubercles were easily visible measuring from 1 to 6 mm. in diameter (Figs. 5-*B*, 6-*A* and 7-*A*). The lesions in the latter two animals were confluent and ulcerative (Fig. 5-*A*). Dogs 688 E and 246 E showed no gross lesions, but small compact

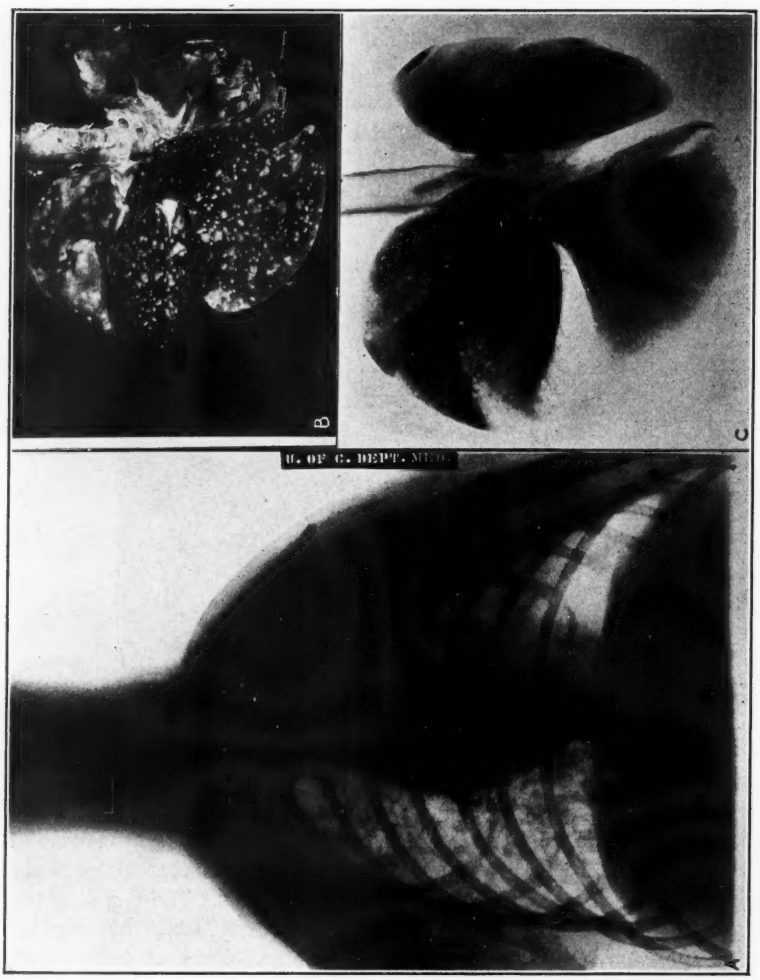

Fig. 5.—(682 E) *A*, X-ray of chest of animal in unilateral hematogenous group. Infected for eight weeks with collapse of infected side for four weeks. Note marked involvement of noninjected side. Injected left lung is collapsed and shows no evidence of tuberculosis.

B, Photograph of lungs of same dog as in *A* sixty-eight days after infection and thirty-nine days after collapse of the left lung. The dog died of massive involvement of the right noninjected lung, exhibiting no gross evidence of tuberculosis of the injected collapsed left lung.

C, X-ray picture of lungs described in *B*, confirming the findings on gross inspection.

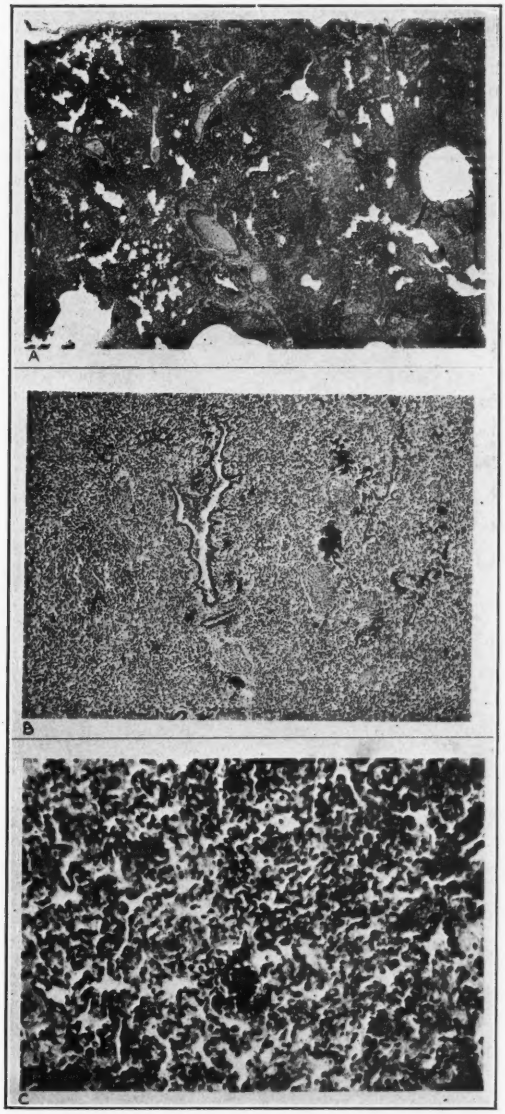

Fig. 6.—(682 E) *A*, Photomicrograph of inflated lung of dog described in Fig. 5-*B*. Many large coalescent tubercles with liquefied caseating centers are demonstrable.

B, Photomicrograph of collapsed lung of dog described in Fig. 5-*B*. Note one small tubercle (A), only three of which were found in the entire section.

C, H. P. photomicrograph taken from section seen in *B*, showing the large number of capillaries present in the collapsed pulmonary tissue.

tubercles were visible microscopically. In general, the tubercles consisted mainly of epithelioid cells, but in those animals where infection was of short duration small round cells, large mononuclear cells and polymorphonuclear leucocytes were more prominent. The tubercles of the longest

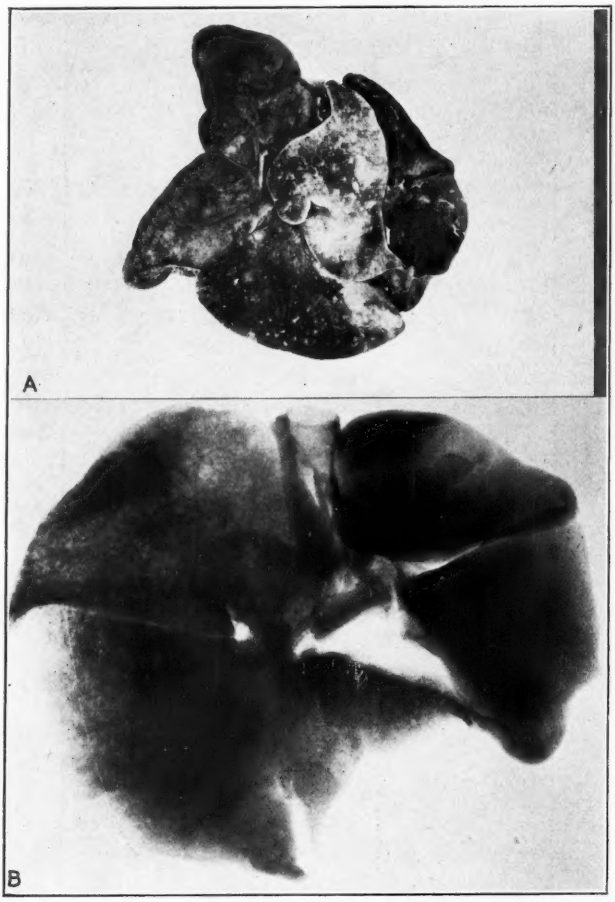

Fig. 7.—(685 E) *A*, Lungs of dog in unilateral hematogenous group. Infected ninety-six days. Left lung collapsed sixty-seven days. Note massive tuberculosis of noninjected right lung, and no evidence of tuberculosis of the atelectatic injected left lung.

B, X-ray picture of lungs described in *A*, confirming the findings of gross inspection.

infected animals, 688 E and 247 E, were more compact, contained much black and brown pigment, and the structure of their cellular units was indistinct. Tubercle bacilli were numerous in the lesions of animals where infection was of short duration. In others, however, particularly

dogs 688 E and 247 E, bacilli were difficult to find, and in dog 126 F both tubercles and bacilli were absent.

The collapsed lobes of the originally infected left lung revealed no gross evidence of tuberculosis as illustrated in the experiment shown in Fig. 6. The tissue of dogs 683 E, 682 E, 246 E and 688 E presented only microscopic tubercles that were difficult to find because of the compactness of the surrounding atelectatic tissue (Fig. 5-*B*). No more than four such tubercles were ever found in a single section. In animals 683 E and 682 E, where infection and collapse were of short duration, the tubercles were composed mainly of epithelioid cells. Lymphocytes and large mononuclear cells were also present, but few in number. In dogs 246 E and 688 E the tubercles were small, compact and composed of epithelioid cells and masses of pigment. Dogs 247 E and 126 E, where infection and collapse were of longest duration, revealed only small collections of lymphocytic cells and pigment, but definite tubercle formation was absent. Tubercle bacilli were difficult to find in all collapsed tissue examined. Occasionally, in animals where collapse was of short duration, one or two bacilli would be found within an epithelioid cell.

SUBPLEURAL

Encouraged by the results in the preceding experiments, and in view of the difficulty and occasional inability to collapse many pulmonary tuberculous cavities by present-day methods, it was thought advisable to evaluate the effect of this simple procedure upon cavities produced experimentally. Seven dogs were used. To obtain such lesions 0.1 to 0.2 c.c. of a heavy suspension of tubercle bacilli in lipiodol[21] was deposited 1.5 cm. beneath the pleural surface of each of three lobes through a thoracotomy opening on the right side. The lipiodol was used to keep the infection localized. One or two of these infected lobes were collapsed from three to eight weeks following infection by bronchial stenosis. One application of silver nitrate was sufficient in each instance. The remaining infected noncollapsed lobes in the same animal thus served as a control. The infecting dose of bacilli was accurately controlled only so far as each lobe injected in a single animal received an equal amount of the same suspension. To bring about still greater unification of results, four animals were infected with an equal amount of the same suspension. This afforded an opportunity to study the evolution of cavities and to observe the effect of collapse upon them as compared with the cavities in the noncollapsed lobes of the same animal.

The postoperative course was followed by frequent fluoroscopic and x-ray examinations. Massive atelectasis was not produced until x-ray evidence of a lesion was obtained. Cough was a more common symptom in this, than in the preceding series. Also the animals appeared more

ill and for a longer period of time than those of the unilateral hematogenous group.

Results.—Three dogs died at periods of eleven, eleven and nineteen days, respectively, following infection, as a result of a bilateral tubercu-

TABLE III

SUBPLEURAL GROUP

DOG NO.	TIME SINCE INOCULATION	DURATION OF COLLAPSE	RESULTS	
			INFLATED	COLLAPSED
101 F	3 months	9 weeks	Dog died of tuberculous empyema right. Right upper and middle were atelectatic. Right lower collapsed by compression. No gross tuberculosis in any lobe. Tubercle B. found in visceral pleura.	
962 E	5 months	3 months	Right lower. Thick-walled cavity 4 cm. in diameter. Miliary tuberculosis of left lung. Numerous microscopic cavities. Many tubercle B.	Right upper and middle. No cavities. Diffuse cellular infiltration. Many tubercle B.
105 F	6½ months	5¾ months	Cavities 2 cm. and 1.25 cm. in right lower and middle lobes. Few tubercle B.	Right upper small cavity (0.5 cm.) containing mucus. Few tubercle B.
104 F	9¾ months	8½ months	Right lower contains a cavity (1.5 × 1 cm.). No tubercle B.	Right upper and middle collapsed. No cavities or gross infection. No microscopic tubules or tubercle B.
998 E	11 days	None. Not cauterized.	Bilateral pleural effusion. Tubercles at site of infection. No cavity.	Some collapse due to compression.
999 E	11 days	None. Not cauterized.	Bilateral pleural effusion. No tubercles at site of infection. Some epithelioid infiltration. Tubercle B. present.	Much collapse due to compression.
997 E	19 days	None. Not cauterized.	Bilateral pleural effusion. Cavities with thick walls at site of injections (½ to ⅔ cm.). Tubercle B. present.	

lous empyema. No cautery had been applied in these cases. At autopsy, varying degrees of compression of the right lung were found. Another (101 F) died three months following infection and nine weeks subsequent to collapse, of right tuberculous empyema. The upper and middle lobes were atelectatic. The right lower was almost completely collapsed due to compression. Tubercle bacilli were demonstrable in the visceral pleura, which was covered by much fibrinous exudate. The remaining animals were sacrificed from five to ten months following infection. The inflated control lobes revealed extensive tuberculous involvement with

cavity formation of 1.0 to 3.75 cm. in diameter in each case. The type of lesion depended largely upon the age of infection. In those dogs where infection was of short duration, as 998 E and 999 E, the response was with tubercle formation. The cells making up these tubercles were predominantly of the epithelioid and large mononuclear types. Many small round cells, lymphocytes and plasma cells were present. Polymorphonuclear leucocytes were diffusely infiltrating the lesions, but in no case were they predominant. Many tubercles showed central looseness of structure and cellular distortion. Others showed a minimal amount of central necrosis, but distinct caseation was not so prominent as in the tubercles of the hematogenously infected animals.

The cavities observed (Fig. 8-*C*) in the remaining dogs, 997 E, 962 E, 105 F and 104 F, were of three main types: those interpreted as early, where the excavation was small and not confined by a fibrous tissue wall; a second type, where the excavation was more pronounced and surrounded by a thick inner wall of cells and a thin outer layer of fibrous tissue; a third type, where the excavation was minimum and limited by a very thin wall of fibrous tissue. The cells making up the wall in the first two types were mainly epithelioid and large mononuclear in character. Small round cells, lymphocytes and plasma cells were also abundant. Polymorphonuclear leucocytes varied in amount, being more numerous in some lesions than in others. Accumulations of these cells were never observed. In general, they had evenly infiltrated the lesion.

Tubercle bacilli were numerous in the majority of disease foci in the inflated lobes, and especially in those of dog 962 E where they were present in quantities comparable to a true culture of the organism. In this animal bronchogenic disseminated tuberculosis of the opposite lung had resulted by spread of the infection from a huge irregular thick-walled cavity in the noncollapsed, control lobe (Figs. 8-*B* and *C*). Dog 104 F, although possessing a huge type three cavity, presented no demonstrable bacilli.

Of the five collapsed lobes, only one contained a very small cavity. In 962 E, cavity was not present but the tissue was diffusely infiltrated with large epithelioid and mononuclear cells. Dog 105 F presented a small cavity filled with mucus. The walls of this cavity were thin and contained remnants of bronchial epithelium. Dog 104 F presented no gross or microscopic tuberculous lesions.

Tubercle bacilli were numerous in the tissue of dog 962 E. In sections of dog 105 F, however, bacilli were few, and in those of dog 104 F organisms were not found.

Fibrous tissue was slightly increased in all sections, being mainly concentrated in the thickened pleura of dog 101 F and about the collapsed bronchi of the remainder.

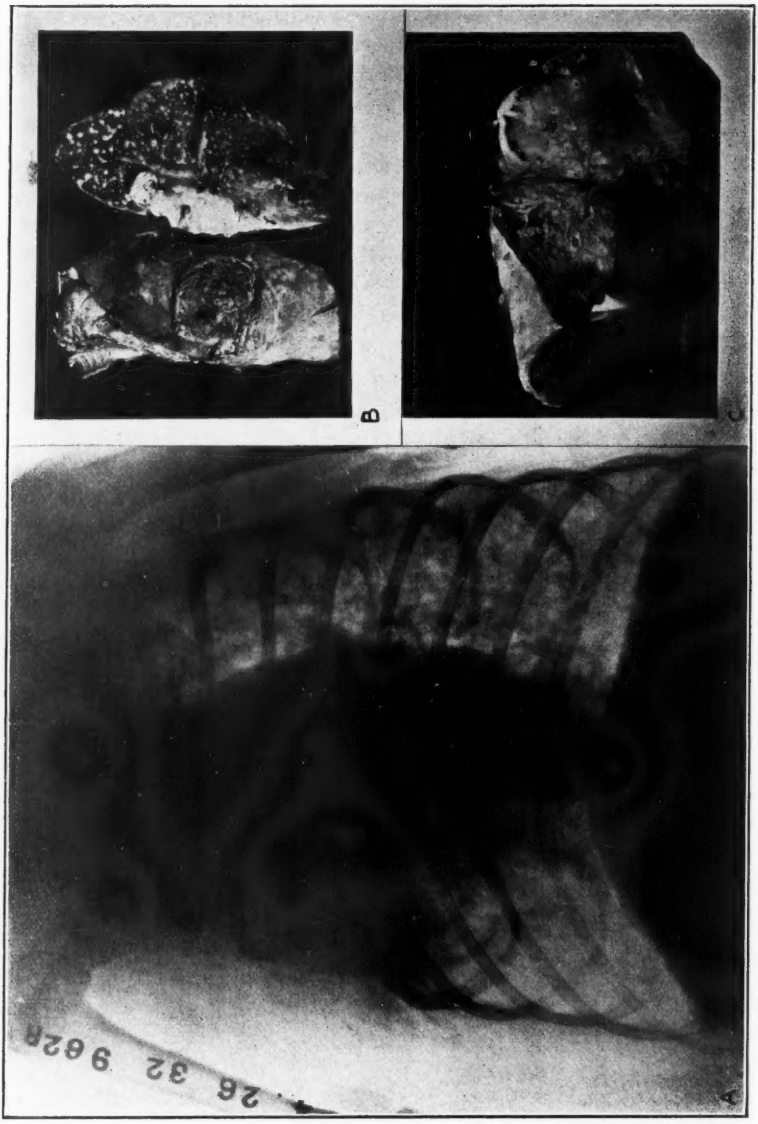

Fig. 8.—(962) *A*, X-ray picture of chest of animal in subpleural group. Infection of right upper, middle and lower lobes was of 4.5 months' duration. Collapse of the right upper and middle lobes, 2.5 months' duration. Note large cavity in right lower lobe (noncollapsed) and miliary tuberculosis of the left lung. The heart is deviated toward the right.

B, Lungs of dog dying two weeks following taking of x-ray picture seen in *A*. There is gross evidence of tuberculosis of all inflated lobes only. Mediastinal glands are much enlarged. On cut section the collapsed lobes contained no cavities. The right lower lobe contained a huge cavity (see *C*).

C, Right lower lobe of lungs seen in *B*, showing huge irregular shaped, thick-walled cavity with remnants of blood vessels only remaining.

Thus, in this, as in the hematogenous series, definite improvement, and in two instances a complete cure, of the lesion was effected by the production of massive atelectasis of the affected part.

BRONCHOGENIC

Up to this period our treatment had been confined to nondraining lesions. That is, the bronchi of the affected lobes were quite clean and were not draining tuberculous processes. Although little success had attended many attempts to produce bronchogenic lung abscesses in dogs, it was thought worth while to attempt to produce lesions somewhat analogous to those seen in human tuberculosis; viz., infiltrating lesions with cavities draining into the tracheobronchial tree. Lipiodol was again used in an attempt to keep the organisms localized. This series of dogs was divided into two groups. In one group of eight dogs, lesions were produced in both lower lobes with the subsequent occlusion of the primary bronchus of one, the other remaining as a control. In the second group of eighteen dogs, a tuberculous lesion was produced in a single lobe, usually the right lower. The bronchus to this lobe was subse-

TABLE IV

BRONCHOGENIC—BILATERAL GROUP

DOG NO.	TIME SINCE INOCULATION	TIMES CAUTERIZED	DURATION OF COLLAPSE	RESULTS	
				INFLATED	COLLAPSED
831 E	7¾ months	5	2¾ months	Cavity 1 × 1.5 cm. Occasional tubercle B.	Cavity 0.5 × 0.75 cm. Very few tubercle B.
109 F	11 months	5	8 months	Thin-walled cavity, 1 × 2 cm. Also indurated mass 1.5 cm. diameter. Many large tubercles. Tubercle B. seen.	No cavity. Some epithelioid cells. No tubercle B.
102 F	11 months	2	9⅓ months	Cavity 1.5 × 2 cm. No tubercles. No tubercle B.	Calcified healed lesion. Epithelioid cells. No tubercle B.
959 E	11 months	1	9½ months	Healing lesion 0.75 cm. diameter. Many caseating tubercles. Few tubercle B.	Healed lesion (grossly). Few small tubercles. Very occasional tubercle B.
961 E	5 weeks	1	None	No collapsed lobe. Lesions 1.5 cm. diameter in each lower lobe. Both contain a cavity. Several tubercles 2-4 mm. in other lobes. Many tubercle B.	
107 F	12 days	0	None	Localized induration. Cellular infiltration. Few tubercle B.	None
108 F	17 days	1	None	Pyramidal shaped indurated areas 2.5 cm. × 4 cm. with central liquefaction in both lower lobes. No collapse. Tubercle B. easily found.	

TABLE V

BRONCHOGENIC—UNILATERAL GROUP

DOG NO.	TIME SINCE INOCULATION	TIMES CAUTERIZED	DURATION OF COLLAPSE	RESULTS
91 F	8 months	4	6 months	Atelectatic. Dense scar at site of lesion 1 × 1 cm. Calcification. Microscopic tubercles. Very occasional tubercle bacillus.
94 F	10½ months	3	8¼ months	Atelectatic. Very dense scar at site of lesion 1.5 cm. Calcification. No necrotic material. Epithelioid cells. No tubercle B.
93 F	10½ months	1	Partial 10 months	Incomplete stenosis but plugged with mucus. Atelectatic except at periphery. Mass 1.5 cm. at site of lesion. Cavity 0.75 cm. 1 tubercle B.
410 F	11 months	7	6¼ months	Incomplete stenosis of the bronchus. Cavity 1.25 cm. No atelectasis. Cellular infiltration about cavity. No tubercle B.
106 F	13⅓ months	7	Partial 9½ months	Incomplete stenosis plugged with secretion. Three-quarters collapsed. Solid lesion with scarring. Microscopic tubercles. Cholesterol slits. No tubercle B.
89 F	13⅓ months	1	12¾ months	Atelectatic. Healing lesion with dense scar. tuant mass 2.5 × 4 cm. filled with mucus at site of lesion. Microscopic tubercles. No tubercle B. Calcium deposits.
92 F	13⅓ months	4	None	Normally inflated. Incomplete stenosis. Cavity 1.5 cm. diameter. No tubercle B.
413 F	16½ months	7	11½ months	Atelectatic. Healed lesion. No tubercles. No tubercle B.
415 F	16¾ months	5	12 months	Atelectatic. Healing lesion with dense scar. Cellular infiltration in region of scar but no tubercle B. Abscess cavity in adjacent aerated lobe. Guinea pig injected with material from this abscess was positive for tuberculosis.
416 F	16½ months	6	12¾ months	Atelectatic. Healed lesion with dense scar. No microscopic tubercles. No tubercle B.
414 F	16½ months	3	14½ months	Atelectatic. Healed lesion with dense scar. No microscopic tubercles. No tubercle B.
411 F	17 months	5	13⅓ months	Atelectatic. Cavity 2 cm. containing thin fluid. No tubercle B. Guinea pig inoculated with fluid was negative for tuberculosis.
423 F	18 days	1	None	Inflated. Cavity 3 cm. diameter with wall 0.6 cm. thick. Much caseation. Many tubercle B.
418 F	38 days	2	None	Bilateral pyothorax. Perforated abscess cavity 3 cm. diameter with thick wall. Many tubercle B.
425 F	56 days	3	None	Inflated. Irregular shaped cavity 4 cm. diameter. Some spread to other lobes. Many tubercles and tubercle B.

TABLE V—CONT'D

DOG NO.	TIME SINCE IN-OCULATION	TIMES CAU-TER-IZED	DURATION OF COLLAPSE	RESULTS
417 F	3 months	4	None	Inflated. Irregular shaped cavity 4 cm. diameter. Several other lobes presented miliary tuberculosis. Many tubercle B. present.
419 F	3½ months	5	None	Pyothorax with perforated abscess cavity 4 cm. diameter with thick, friable wall. Miliary tuberculosis in one other lobe. Many tubercle B.
Goat	14⅔ months	3	11⅔ months	Left lung collapsed. Much scarred at site of lesion. No cavity. Microscopic tubercles. Multiple calcium deposits. No tubercle B.

quently occluded. Three monkeys were added to this series, and also three goats. However, due to technical difficulties and to the extreme susceptibility of the monkey to the organism used, all three died before collapse therapy could be instituted. This was also true in the case of two of the goats.

The tuberculous lesions in the entire series were produced in the following manner.[22] Dogs: Under morphine anesthesia and fluoroscopic control, a bronchoscope was passed. A ureteral catheter was then introduced into the finer ramifications of an air passage (at any desirable location), and 0.2 c.c. of a heavy suspension of human tubercle bacilli (H 119) in lipiodol deposited. Monkeys and Goats: Ether or barbital was necessary as an anesthetic agent and from 0.3 to 0.5 c.c. of the suspension was used instead of 0.2 c.c. Otherwise the procedure was the same as in dogs.

The course of the lesions produced was closely followed by fluoroscopy, bronchoscopy and roentgenography. Complete stenosis of the primary bronchus of the affected lobes, with massive atelectasis of the obstructed lung tissue, was produced from three weeks to five months following infection. More coughing was observed in this than in the preceding series. In some cases it was extreme. Drainage of the lesion into the tracheobronchial tree was universal. In some cases this was enormous, and here it was impossible to occlude the draining bronchus completely until drainage had partially subsided. The failure of occlusion was thought to be due in part to dilution of the cauterizing agent by both the exudate and the edema of the bronchial mucosa. As a result, the cauterization frequently had no effect upon the diameter of the bronchial lumen. Thus, as shown by Tables IV and V, repeated applications of the cautery were necessary in most cases to effect complete closure of the draining bronchus.

Results.—A summary of the results of this series is shown in Tables IV and V. Cavities from 1.5 to 3.5 cm. in diameter were routinely produced and were many times demonstrated on x-ray examination. In the bilateral group, similar to the subpleural series, the animals with one infected lobe untreated by collapse appeared ill and were less active than those of the unilateral group where all of the diseased lung had been collapsed. This was also true of those animals of the unilateral group which received no collapse. On the whole we were successful in keeping the tuberculous lesions confined to the desired locations. There was a spread of the infection to neighboring lobes in only four cases. This was a bronchial dissemination in one, and a diffuse infiltration in the other three.

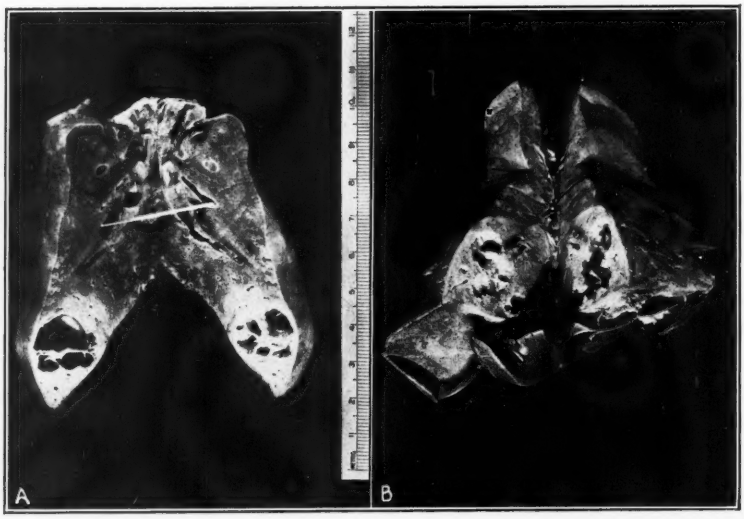

Fig. 9-*A*, (423 F) Lower lung lobe of dog in unilateral bronchogenic group. Infection, eighteen days' duration. No collapse. Note large trabeculated thick-walled cavity.

B, (425 F) Lung of dog in unilateral bronchogenic group. Infection of lower lobe for two months. No collapse. Note large irregular-shaped thick-walled cavity in lower lobe. There was a spread of the infection to other lobes in the form of a diffuse infiltration.

Of the seven dogs in the bilateral group, three died at 12, 17 and 35 days respectively, before any collapse had been produced. Two had received one application of the cautery, the third had received none. Localized tuberculous lesions were found in three of the dogs, with cavity formation in two. The remaining four dogs were sacrificed at 7.75, 11, 11 and 11 months following infection. Three exhibited unhealed cavities in the inflated (control) lobe; whereas only one presented a cavity in the collapsed lobe, this being about one-half the size of the cavity in the control inflated lobe in the same animal.

In the inflated lobes the tuberculous process could be divided into various types, as follows, depending upon the duration of infection. Cavitation, however, was the rule if the dog survived and the infection progressed for as short a period as seventeen days (Figs. 9-*A* and *B*).

Type 1—Cellular Reaction Without Caseation or Cavity.—At the site of lodgment of the tubercle bacillus suspension there was a purulent bronchitis with peribronchial infiltration of cells mainly polymorphonuclear in type. Lymphocytes and large mononuclear cells were present in small amounts. The alveolar walls were slightly thickened by small round cells. Tubercle bacilli were numerous.

Type 2—Caseation and Early Cavity With a Thick Inner Wall of Cells and a Thin Outer Wall of Fibrous Tissue.—In the caseous areas there were many small

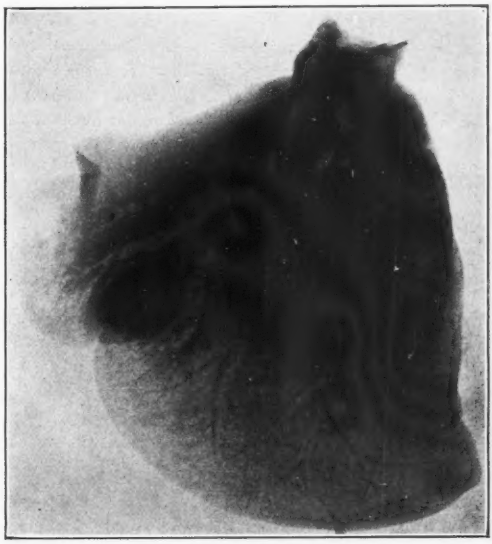

Fig. 10.—(93 F) X-ray picture of lower lobe with bronchogenic infection of 10.5 months' duration and partial collapse of lobe for 10 months. (Incomplete stenosis of main bronchus and plugging with mucus accounted for the partial collapse.) Note circular calcified shadow with retraction of the periphery of the lung at that point. On cut section a small abscess cavity was found.

cells unrecognizable because of necrosis. The cells making up the wall were mainly of the epithelioid and large mononuclear cell types. Large and small round cells and plasma cells were also prominent. Polymorphonuclear leucocytes were abundant and in the majority of cases evenly distributed except in dog 108 F where they had collected in numerous small masses. The lung tissue of this latter animal, however, was infiltrated throughout with polymorphonuclear leucocytes and tuberculous pneumonia was evident. Tubercle bacilli were concentrated in the thick inner wall of cells.

Type 3—Large Cavity With Thick Walls of Fibrous Tissue.—Cavities of this type were generally greatly dilated and traversed by bands of fibrous tissue and thrombosed vessels. In most cases the cavity communicated with the lumen of a neighboring bronchus (in this respect they differed from those of the subpleural group where communication with bronchi was not always evident). At such points of

union, bronchial mucosa made up a minor portion of the wall, but as one approached the true cavity the epithelial lining stopped abruptly and gave place to dense fibrous tissue. This wall and the immediate surrounding lung parenchyma were infiltrated with a few lymphocytic and large mononuclear cells. Bacilli were not numerous in tuberculous foci of this type, and none were observed in the cavity wall of dog 102 F.

Type 4—No Cavity but Microscopic Fibrotic Tubercles and Large Amounts of Fibrous Tissue Throughout the Pulmonary Parenchyma.—This was observed in dog 959 E, where infection and collapse were of longest duration. The tuberculous process was represented mainly by tubercles, some with caseation and others in which cell death was at a minimum. The latter tubercles were solid and contained varying amounts of fibrous tissue. Few bacilli were observed in such tubercles. Collapsed lobes were obtained in only four animals of this group and in these cautery had to be applied many times before stenosis of the bronchus resulted. The tuberculous process in these lobes was decidedly smaller than that in the corresponding inflated control lobes. Dog 831 E, where collapse was of shortest duration, presented a small cavity with a thick wall in which few tubercle bacilli were observed. In the other three animals, where infection and collapse were of longer duration, evidence of regression and healing was present. In dog 109 F cavitation was absent, but the tissue was generally evenly infiltrated with large mononuclear and epithelioid cells. These cells were occasionally massed together in tubercle formation. Neither cell death nor caseation was evident in such areas, and bacilli were not numerous. Dog 959 E presented few small compact epithelioid tubercles, some with small amounts of central caseation, others with none. Many such tubercles were surrounded by a dense layer of small round cells and masses of pigment. Others were infiltrated and enclosed by fibrous tissue. In dog 102 F, at the site of the original cavity (as demonstrated by fluoroscopy during life) there was much scar tissue with microscopic calcification and bone formation.

Few tubercle bacilli were found in sections of dogs 831 E, 109 F and 959 E. They were always less numerous than in the corresponding inflated lobes. In dog 102 F bacilli were not found.

Of the seventeen dogs in the unilateral group, five died and twelve were sacrificed. The five died from 18 days to 3.5 months following infection, all presenting a cavity 3 to 4 cm. in diameter. These had received from one to five applications of the cautery with resultant incomplete occlusion of the bronchus and thus no collapse of the pulmonary tissue. Many tubercle bacilli were demonstrable in each case. The twelve dogs sacrificed will be described in more detail.

Dog 91 F. Infected eight months and collapsed six months. Presented a dense scar at the site of the original injection with deformity of the normal contour of the lobe. An x-ray picture revealed calcium deposits in this area. The entire lobe was atelectatic. On microscopic examination small tubercles containing an occasional tubercle bacillus were seen.

Fig. 11.—(94 F) *A*, X-ray picture of chest of dog with bronchogenic infection of right lower lobe for two months. Complete stenosis of the right lower lobe bronchus with collapse of the lobe—of a few days' duration. Note deviation of the heart to the right with definite tuberculous involvement of the right lower lobe.

B, X-ray picture of chest of same dog as in *A*, taken 5.25 months after bronchogenic infection of right lower lobe and 3.5 months following collapse of the same lobe. Note contrast in size of lobe to that seen in *A*.

C, X-ray picture of right lower lobe of dog described in *A* and *B*. Infected 10.5 months, collapsed 8.25 months. Note airless condition of pulmonary tissue and retraction of periphery of lobe in region of calcified shadow. Much scarring was present in this region, and on cut section no cavity was found.

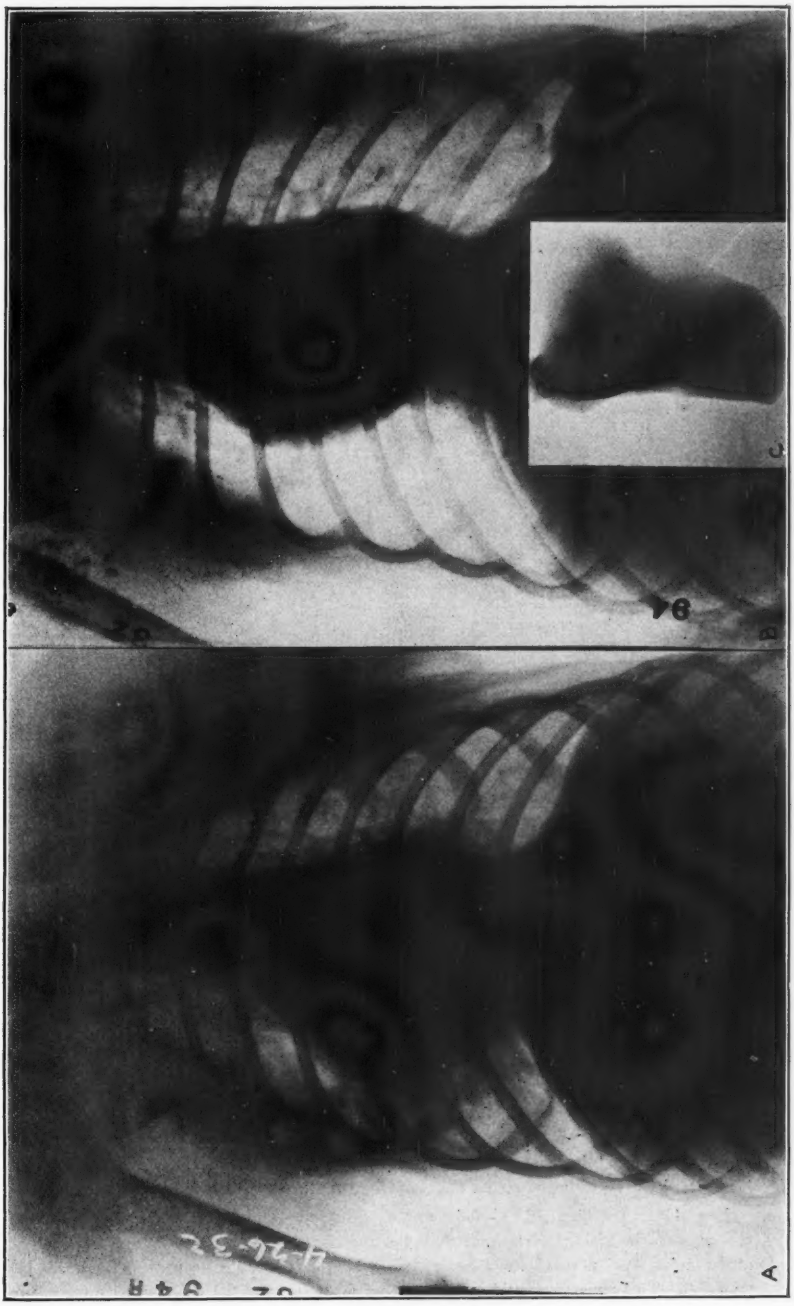

Fig. 11.—*(See opposite page for explanation.)*

Dog 94 F. Infected 10.5 months and collapsed 8.25 months. The entire lobe was atelectatic and presented a circular dense scar at the site of the original infection, with marked deformity of the lobe in this region. No cavity was demonstrable. X-ray film again revealed calcification in the region of the scar (Fig. 11). Only a few epithelioid cells were found on microscopic examination and no tubercle bacilli could be demonstrated.

Dog 93 F. Infected 10.5 months, collapsed (partially) 10 months. The lobe was atelectatic except at the periphery. There was considerable scarring at the site of the lesion with deformity of the lobe (Fig. 10). A cavity 1.75 cm. in diameter remained. Microscopic tubercles were demonstrable, and one tubercle bacillus was seen.

Dog 106 F. Infected 13.33 months and collapsed (partially) 9.5 months. Again the lobe was atelectatic except at the periphery. Both dog 93 F and dog 106 F presented an opening 1.0 mm. in diameter in the primary bronchus of the lobe, which was plugged with mucus. Thus incomplete atelectasis resulted. Again a solid lesion with much scarring was found. Microscopic tubercles and many cholesterol slits were demonstrable. No tubercle bacilli were seen.

Dog 89 F. Infected 13.3 months and collapsed 12.75 months. Entire lobe atelectatic. At one side of the lobe a fluctuant mass 2.5×4 cm. was found to contain mucus and a small amount of caseous material. Microscopic examination revealed diffuse cellular infiltration of the lobe, but no tubercle bacilli were found. An x-ray picture again showed calcium deposited in the fluctuant area.

Dog 92. Infected 13.3 months. There was incomplete occlusion of the bronchus with no collapse of the pulmonary tissue. A smooth walled cavity 1.5 cm. in diameter was found. No tubercle bacilli were demonstrable.

Dog 410. Infected 11 months and collapsed 6.25 months. Died of poisoning. There was incomplete stenosis of the right lower lobe bronchus with no atelectasis. A cavity about 1.25 cm. in diameter was present which on microscopic examination revealed much infiltration with lymphocytes and endothelial cells. Stains revealed no tubercle bacilli.

Dog 411. Infected 17 months and collapsed 13.3 months. The infected lobe was atelectatic and contained an abscess cavity 2 cm. in diameter which contained a fairly thin turbulent fluid. A guinea pig inoculated with this was negative for tuberculosis and cultures were sterile. The cavity was lined by a caseous-like material. Stains for tubercle bacilli were negative.

Dog 413. Infected 16.5 months and collapsed 11.25 months. The entire right pleural cavity was obliterated except for a pocket filled with about 2 to 3 ounces of a thin turbid fluid. The entire right lung was collapsed, the right lower being atelectatic due to complete stenosis of its bronchus and the upper two lobes collapsed by the preexisting empyema. This empyema had been aspirated repeatedly. Guinea pigs injected with fluid aspirated had been positive for tuberculosis. A dense scar was seen in the right lower at the site of infection. Microscopic sections revealed no tubercles or tubercle bacilli. Microscopic sections of the wall of the empyema cavity revealed no tubercle bacilli.

Dog 414. Infected 16.5 months and collapsed 14.25 months. The infected lobe was completely atelectatic and presented much scarring in the region of the lesion. Microscopic sections revealed no tubercles or tubercle bacilli.

Dog 415. Infected 16.75 months and collapsed 12 months. The infected lobe was atelectatic with much scarring in the region of the previous lesion. The right upper lobe was aerated and contained multiple abscesses containing semiliquid material. There was a considerable amount of induration of the tissue surrounding

the abscesses. A guinea pig injected with material from these abscesses was positive for tuberculosis. Microscopic sections of the atelectatic lobe revealed no tubercles or tubercle bacilli.

Dog 416. Infected 16.5 months and collapsed 12.75 months. The infected lobe was atelectatic and presented a massive scar in the region of the former cavity. Microscopic sections revealed no tubercles or tubercle bacilli.

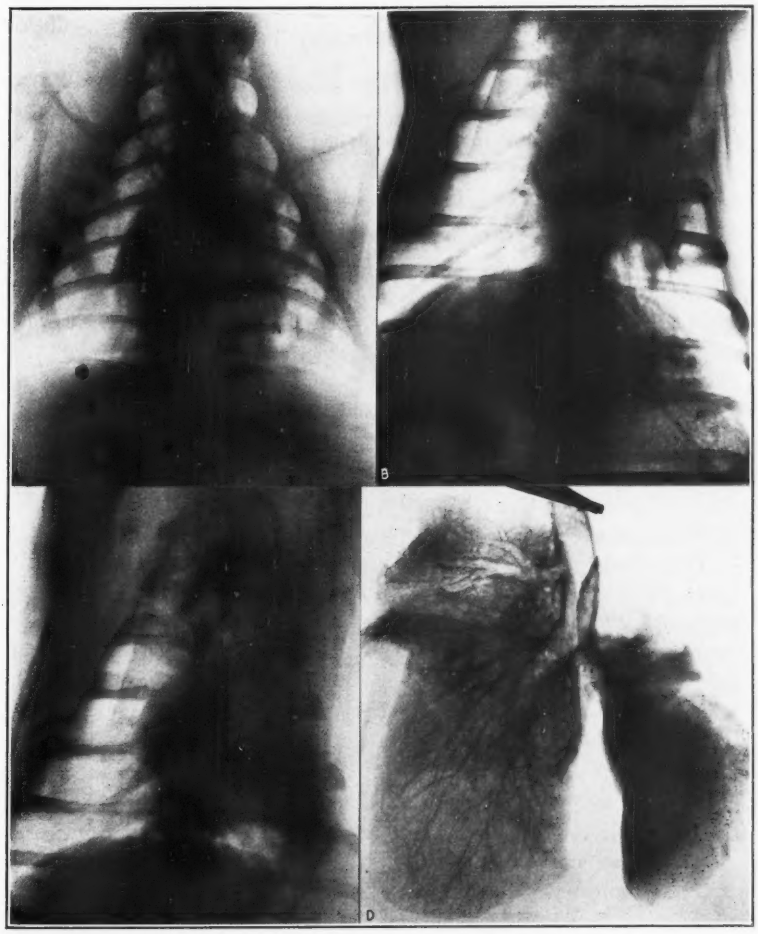

Fig. 12.—Goat. *A*, X-ray picture of chest of goat one month following bronchogenic infection of left lower lobe. Note annular shadow (A) just below and lateral to heart.

B, X-ray pictures of chest of same goat taken three months following infection and a few days following massive collapse of the entire left lung. Note marked collapse of left lung and large spontaneous pneumothorax (left).

C, X-ray picture of chest of same goat taken fifteen months following infection and twelve months following collapse of left lung. The left lung is airless, and the heart is deviated toward the left chest.

D, X-ray picture of lungs of same goat. Infected fifteen months. Collapsed twelve months. Note massive atelectasis of entire left lung with calcium deposits throughout. Only a scar remained where cavity once was demonstrated.

Goat A. Infected 14.6 months, collapsed 11.6 months. The left lung was completely atelectatic and a scar remained at the site of the original lesion. An x-ray film revealed bits of calcium deposited throughout the collapsed lung (Fig. 12). Minute tubercles with giant cells were present on microscopic examination, but no tubercle bacilli could be found.

The other two goats died too early in the experiment to be worthy of report, as did also the three monkeys.

DISCUSSION OF RESULTS

The routine regularity of production of tuberculous lesions by all three methods used is of very great importance. This being true, the effect of collapse on these lesions could be extremely well controlled and evaluated.

In some early experiments of the hematogenous group it was found that a very few minute tubercles were produced in already atelectatic lobes. However, in contrast to the inflated lobes, atelectatic pulmonary tissue was a very poor medium for the growth of tubercle bacilli.

The marked contrast between atelectatic and inflated lobes in the bilateral hematogenous group a few weeks following infection was most surprising. This was especially true when one considered the fact that the destruction in inflated lobes and the healing of the lesions in the collapsed lobes were taking place simultaneously in the same animal.

That rest of the part as well as chemical changes plays an important rôle in the treatment of pulmonary tuberculosis was brought out by the three animals exhibiting a physiologic anastomosis[23, 24] between two lobes. This finding of anastomosis between two lobes was in contradistinction to Van Allen's[25] belief that "collateral respiration" occurred only between lobules of a lung lobe. We have observed this condition in six dogs, including three others outside of this series. Although tuberculous lesions persisted in these lobes (partially aerated, but with the main bronchus completely stenosed), they were far less extensive than those lesions seen in normally inflated lobes with their bronchial lumen patent. On the other hand, the lesions were much more advanced than those persisting in the collapsed lobes.

We were only partially successful in keeping the infection confined to one lung in the unilateral group of the hematogenous series (injection via the pulmonary artery branch). Here again, the contrast between the atelectatic and normally inflated tissue was very marked in those cases where the inflated side became infected (see Fig. 5). Usually, however, the amount of infection of the noninjected lung was so small that the animal appeared quite well a few weeks after collapse of the injected side.

Of the eight dogs in the subpleural group, three developed pleurisy with effusion due to rupture of a lesion produced near the surface of the lung. The dogs died subsequently due to mechanical compression of both lungs.

Lesions produced by this method were much more severe than those in the preceding series, and of necessity needed a much longer period of time to exhibit beneficial effects from collapse. However, in this series as in the hematogenous, definite healing or attempts at healing were manifested following occlusion of the main bronchus and the production of massive collapse of the entire lobe. In one case there was an exceptionally interesting phenomenon. After the dog had been infected for 4.5 months and two of three lobes had been collapsed for 2.5 months, there was definite x-ray evidence of the onset of miliary tuberculosis of the remaining inflated pulmonary lobes. The dog was sacrificed two weeks later. Autopsy confirmed the x-ray findings (Fig. 8). The control lobe (noncollapsed) presented a huge, irregularly shaped cavity with a thick, partly necrotic wall traversed by remnants of blood vessels. The miliary spread was quite likely a bronchial dissemination from the control cavity. No cavities were found in the collapsed lobes.

Very large localized lesions were again produced in the bronchogenic series, and longer periods of time were needed for healing. Many cases developed lesions from which drainage was profuse. Thus complete occlusion of the draining bronchus was not obtained for several weeks, and several animals died before collapse could be produced (Fig. 9). After collapse had been instituted for several months, much more local scarring of the lung was found than in the specimens of either of the other two series. This scar produced considerable disfiguration of the atelectatic lobe. Another interesting finding was the deposition of calcium at the site of the original lesion which cast a shadow in the x-ray picture. This was identified by chemical analysis and microscopic examination. Two dogs presented incomplete occlusion of the bronchus with plugging of the remaining opening by mucus. The lobe of each was incompletely atelectatic. Although there was definite fibrosis and healing of the lesion, it was not nearly so advanced as in the completely collapsed lobes. The deposition of calcium was also noted in these specimens but to a less degree.

Dog 89 presented a very interesting condition. A large, thin-walled, fluctuant mass was attached to one side of a completely atelectatic lobe. It contained much mucus and a small amount of caseous material. No tubercle bacilli could be found. It is quite likely that an abscess cavity was located near the surface of the lobe and threatened perforation. With closure of the bronchus the cavity was filled by mucus-secreting glands, and became dilated due to an extremely thin wall. It appeared not unlike a mucocele.

Other findings of probable significance were noted in dogs 411 and 415. A guinea pig injected with material from an abscess in the atelectatic lobe of dog 411 failed to develop evidence of tuberculosis. On the

other hand, definite tuberculous lesions developed in a guinea pig injected with material from an abscess in an aerated lobe of dog No. 415.

This series of lesions was more analogous to those found in the human being, viz., cavities from which there was much discharge. The goat in this series responded to collapse by this method in a manner very similar to that of dogs. A large cavity was completely obliterated and bits of calcium were deposited throughout the collapsed lung. Unlike most of the dogs, the infection became diffuse throughout the lobe; hence the failure of concentration of the calcium at the site of the original lesion.

GENERAL DISCUSSION

The primary purpose of this experiment was to note the effects of lung collapse, as obtained by bronchial occlusion, on the experimentally produced pulmonary tuberculosis. Opportunity developed, however, to obtain an estimate regarding some of the factors involved in the production of the disease types from tubercle to cavity.

FACTORS DETERMINING THE TYPE OF LESION

Duration of Infection.—It is evident from the results of this experiment that the type of lesion observed at autopsy depended largely upon the length of time intervening between infection and death of the animal.

Numbers of Bacilli Localized.—In the subpleural and bronchogenic group where large numbers of bacilli were localized by being suspended in lipiodol, early cavitation resulted as a routine. Such excavations were made evident by frequent fluoroscopic examinations, roentgen ray pictures, and in most cases by gross examination of inflated tissue at autopsy. In the intravenous injections, however, where moderate numbers of bacilli evenly suspended in saline were introduced, as in the hematogenous group 1-A, pulmonary tubercles without ulceration were generally observed. It is common knowledge that rarely after such injection will cavitation result, and then only after a prolonged period necessary for multiplication of the bacilli at the site of lodgment. These observations are in accordance with the opinion that numbers of bacilli at any one place at a given time are important in determining the type and site of a tuberculous lesion whether it be tubercle or cavity.

EFFECT OF BRONCHIAL STENOSIS AND COLLAPSE ON TUBERCULOSIS

Throughout the experiment the tuberculous process in the atelectatic lobes failed to progress and, in general, showed evidence of regression and even healing. These results were interpreted as being largely due to death of the contained tubercle bacilli because of inhibition of substances necessary for their growth. Some insight regarding these

growth requirements and how the tubercle bacilli are affected in their decrease or absence may be obtained from adequately controlled cultural methods.

Growth Requirements of Tubercle Bacilli in Culture.—The most discussed of these is the relative need of carbon dioxide and oxygen for life of the bacillus. Wherry and Ervin[26] state that certain optimum percentages of carbon dioxide are necessary for the growth of the tubercle bacillus, and that too low and too high tensions of this gas repress growth. Rockwell and Highberger[27] conclude that carbon dioxide is in some way a vital factor in the growth of tubercle bacilli. Novy and Soule,[28] however, challenge this view of carbon dioxide necessity. According to their interpretation the growth of the organism proceeds in direct proportion to the oxygen tension, "the higher the tension (up to certain limits) the greater is the growth, the lower the tension the smaller and poorer is the growth." Corper, Gauss and Rensch[29] conclude that accumulations of carbon dioxide retard growth of tubercle bacilli in vitro and in vivo. Recently Corper, Lurie and Uyei[30] and Corper and Lurie[31] found a definite relation existing between oxygen tension and the velocity of growth of the organisms and their pathologic process. In studying the availability of oxygen in different organs, they find that after intravenous injection of the bacilli, the growth is faster in the lungs where large amounts of oxygen are available, and slower in the liver where oxygen is present in a much smaller amount.

Loebel, Shorr and Richardson,[32] in considering the growth of human tubercle bacilli (H 37), have shown that complete destruction of the respiratory and growth capacity of the organism followed their cultivation under anaerobic conditions. The period of anaerobiosis necessarily varied according to the type of medium used for cultivation. On Long's nutrient solution it occurred in four days' time, whereas on a nonnutrient solution the capacity to grow was abolished in sixty-eight hours, and to respire in seven days.

These data regarding oxygen and carbon dioxide requirement make it evident that oxygen is a most vital factor in determining the growth of the organism.[33]

Other substances besides oxygen, however, are necessary for growth of the tubercle bacilli on culture medium. Certain inorganic salts, glycerol and water are essential. Of these food substances, glycerol is the most significant for the bacillus. As stated by Long, "without it the tubercle bacillus is on a starvation diet." Its addition to culture medium affords a more luxuriant growth.[34]

Decrease in the Growth Requirements of the Tubercle Bacilli in the Tissue of This Experiment.—Bronchial stenosis with complete occlusion of the lumen by fibrous tissue stops completely the normal respiratory

mechanism of the respective lung lobe. The pulmonary tissue becomes collapsed, airless and solid. What oxygen it receives is carried mainly by way of the oxygenated blood of the bronchial artery. It is also possible that the blood flow through this artery is diminished due to the fibrosis of the bronchial wall at the site of cautery. The impure blood of the pulmonary artery, not having lost all of its oxygen, likewise affords a minute amount. In view of the necessity of this gas for adequate growth on culture medium it seems plausible to conclude that the tubercle bacilli could not thrive in a pulmonary medium of this sort.

Other organs such as lymph node, spleen, liver and kidney, where the oxygen supply is far less than that of a normally respiring pulmonary tissue, frequently harbor a tuberculous process. The lack of oxygen due to stenosis of the bronchus may not entirely account for the death of the contained bacilli.

Incident to the collapse by this method there was also produced a blood stasis or passive congestion of the atelectatic tissue. It was thought, at first, that the large amount of blood observed in the collapsed tissue was due to hemorrhage. There was no evidence, however, of coagulation and destruction of the red blood corpuscles as is commonly seen in blood that has exuded into a tissue space. To show that the normal blood channels in this collapsed tissue were dilated and the tissue was in a state of congestion, India ink, after the method of Coryllos,[17] was injected into the blood stream of dog 847 E. At autopsy the collapsed lung appeared to contain far more ink than the corresponding normally inflated control lobes. This observation of blood stasis is further substantiated by the work of Moore,[35] Moore and Cochran,[36] and Hilton,[37] who noted a decrease in the volume of blood flow per minute through collapsed tissue.

With blood stasis there is a diminished nutritional state. The tubercle bacilli in such tissue are deprived not only of oxygen but also of other growth essentials that reach them through the blood stream. These substances, however, per unit of normal blood never reach the concentrations necessary for the cultivation of the organisms in vitro. It would seem therefore that the bacilli are but little dependent upon blood supply for adequate nourishment. Long[38] has aptly summed up this problem of concentration by the statement, "we must not forget that the nutritional state in the living animal body is one of continuous supply." Also, in speaking of the glycerol concentration, "although never high at a given moment the amount of glycerol reaching a site of bacillary lodgment in the course of a day through the agency of the blood or lymph stream might well compare with the effective concentration in artificial culture."

In conclusion we may say that bronchial stenosis with its subsequent lung collapse and congestion brought about a decrease in the growth

requirements reaching the tubercle bacilli harbored by the atelectatic pulmonary tissue. In this way it favored the death of the contained bacilli and a recession or healing of the disease process.

Stenosis of Bronchi and Prevention of Bronchogenic Spread.—In cases of cavitation with marked productivity, difficulty was encountered in occluding the draining bronchus. Even with numerous applications of silver nitrate such bronchi failed to stenose, and collapse of the corresponding lung tissue was not obtained. Of the probable factors prohibiting occlusion in such instances, two seem to be paramount. The excrement may have diluted and washed away the cauterizing agent or the constant flow of material past the site of cautery maintained the patency of the bronchial lumen. In no case where the bronchus was moderately clean did we fail to obtain stenosis by one or two applications of silver nitrate. Thus the success of bronchial stenosis by this method was directly proportional to the amount of bronchial excretion flowing past the site of cautery.

By closing the bronchus the danger of bronchial dissemination of tubercle bacilli into other healthy lobes is removed. This is often the result in cases where collapse of lobes harboring bronchogenic cavities is induced without closure of the draining bronchus.

In a number of animals of the unilateral bronchogenic group, where draining bronchogenic cavities were present and the bronchus remained open, bronchogenic dissemination of tubercle bacilli had occurred into other healthy lobes not originally infected. At autopsy these lobes showed marked peribronchial tuberculosis. In another animal, dog 962 E, of the subpleural group, the control lobe contained a large irregularly shaped cavity from which bronchial spread into remaining inflated control lobes had likewise occurred. In those cases, however, where the bronchus of the lobe harboring the disease process was occluded, as in dogs 91 F, 94 F, 89 F, 411 F, 414 F, and 416 F of the bronchogenic group, dissemination into other lobes by way of that bronchus was not evident at autopsy.

Closure of Cavities.—Many of the experimental cavities, particularly those of the bronchogenic group, had attained considerable size before the bronchus was successfully closed. After stenosis, however, they gradually regressed as demonstrated by frequent roentgen ray visualizations, and at autopsy only fibrous tissue scars existed at the site of previous cavity. In the normally inflated control lobes, however, cavities were always present at autopsy and much larger than indicated by roentgen ray some days previous to the death of the animal. These results indicate that bronchial stenosis and subsequent lung collapse proved efficient in closing the experimentally produced tuberculous cavities.

CLINICAL APPLICATION

In dogs cauterization of a bronchus with a 35 per cent solution of silver nitrate we have found has not led to a single death in over two hundred instances of application. Due to the fact that others have had some difficulty in obtaining the desired results, the procedure has been described in detail elsewhere.[39] With this factor of safety in mind and in view of the marked beneficial results in pulmonary tuberculosis observed throughout our experiments, it was decided to test its application in human cases of tuberculosis. Only hopeless cases with bilateral involvement have been selected, and at this time few conclusions can be derived. In four cases the cauterizing agent was applied a total of twelve times. In all four cases a considerable amount of sputum had been raised daily. In one case a huge cavity in the right lung communicated with the bronchi of all three lobes. The upper and middle lobe bronchi were completely stenosed with one and two applications of the cautery respectively. The lower lobe bronchus remained open and draining despite two cauterizations. There was no collapse of the right lung. This patient died one and one-half months afterward, and no autopsy was obtained. The other three patients were not under continuous control. All have since died, two having developed intestinal tuberculosis.

Considerably more difficulty was encountered in applying the cauterizing agent properly to the upper lobe bronchus in the human being than in the dog. A specially constructed applicator partially overcame this difficulty.

Another point of importance was the mildness or entire lack of reaction following an application of the cauterizing agent. In several instances there was a temporary improvement characterized by a decrease in daily temperature and sputum. In no case was x-ray evidence of lobe collapse obtained, although in two cases physical signs of the cavity disappeared temporarily following cauterization. This was thought to be due to temporary occlusion of the bronchial lumen.

SUMMARY AND CONCLUSIONS

Atelectasis of pulmonary tissue brought about by bronchial occlusion exerted a favorable influence on experimental pulmonary tuberculosis in dogs, whether induced by hematogenous or bronchogenic infection, or by direct inoculation.

Tubercles in the collapsed lobes were in general small and almost free from bacilli, whereas in inflated lobes in the same animals they tended to be large, often confluent, caseous and rich in acid-fast bacilli.

The favorable effect in the collapsed lobes increased with the duration of the collapse and in some cases amounted to a complete cure of the disease.

This beneficial influence may be attributed to several factors, viz., absolute rest, decrease in oxygen, and increase in carbon dioxide.

Tuberculous lesions were produced with routine regularity either by hematogenous or bronchial infection or by direct inoculation and the influence of collapse on these lesions could be extremely well evaluated.

Little difficulty was encountered in producing complete stenosis of a bronchus not discharging pus. Where a discharge was present, repeated applications of the cautery were necessary to effect complete occlusion.

Bronchi closed in man as readily as in dogs. Little or no reaction attended the application of the cauterizing agent in human cases.

We wish to express our thanks to Dr. Edmund Andrews and Dr. Esmond R. Long for their interest and suggestions in this study, and to Dr. L. E. Dostal and Leo Hrdina for technical assistance.

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Erratum

The cut furnished by the George P. Pilling and Son Company of Philadelphia to illustrate the article by Dr. Milton Sills Lloyd on page 541 of the June issue was in error in representing the length of the catheter as 40 mm. instead of 40 cm. The illustration also failed to show that the cannula and the catheters are graduated by centimeter lines.

American Association for Thoracic Surgery

By special action of the Council the place of the next annual meeting of the American Association for Thoracic Surgery has been changed from Chicago to New York City. The meeting will be held late in May or early in June, 1935. More definite announcement of the dates will be published later.

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